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Award Number: DAMD17-02-1-0252

TITLE: Prostate Can Men: The Effect of Body Habitus and Physical Activity

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REPORT DATE: February 2006

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	February 2006	Final (1 Feb 2002 - 31 Jan 2006)

4. TITLE AND SUBTITLE
Prostate Cancer Mortality in Puerto Rican Men: The Effect of Body Habitus and Physical Activity

5. FUNDING NUMBERS
DAMD17-02-1-0252

6. AUTHOR(S)
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES
Original contains colored plates: ALL DTIC reproductions will be in black and white.

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 Words)
Prostate cancer kills more Puerto Rican men than the combined cancer mortality rates of the lung, trachea and bronchus. The most extensively studied risk factors for prostate cancer include age, race/ethnicity, family history, diet, androgen metabolism, alcohol consumption, obesity, physical activity and smoking. Of these, age, race and family history are well documented but poorly understood risk factors. The fact that prostate cancer rates change in migrant populations and vary dramatically in ethnically similar populations residing in different geographic locations strongly suggest that environmental factors can greatly influence the risk of this cancer. Purpose: The purpose of this investigation is therefore, to study the relationship of physical activity and body habitus with prostate cancer mortality among Puerto Rican men. This study uses an observational longitudinal design with a random sample of 9,824 Puerto Rican men aged 35-79 years at baseline (1964) who were part of the Puerto Rico Heart Health Program (PRHHP Survival analyses will be used to study the relationship between prostate cancer mortality and physical inactivity and obesity with approximately 35 years of follow up data. Scope of the research: This research is to generate new knowledge of how sedentary lifestyles or excess body weight are related to prostate cancer mortality, and to increase our knowledge of prostate cancer in a population where prostate cancer is the number one killer. Additionally, once prostate cancer mortality is identified, other exposures such as diet, smoking and alcohol intake can also be studied.

14. SUBJECT TERMS
prostate cancer, Puerto Rico, physical activity, body habitus

15. NUMBER OF PAGES
91

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Title: Prostate Cancer Mortality in Puerto Rican Men: The effect of body habitus and physical activity

INTRODUCTION:

Subject: Prostate cancer kills more Puerto Rican men than the combined cancer mortality rates of the lung, trachea and bronchus. The most extensively studied risk factors for prostate cancer include age, race/ethnicity, family history, diet, androgen metabolism, alcohol consumption, obesity, physical activity and smoking. Of these, age, race and family history are well documented but poorly understood risk factors. The fact that prostate cancer rates change in migrant populations and vary dramatically in ethnically similar populations residing in different geographic locations strongly suggest that environmental factors can greatly influence the risk of this cancer. **Purpose:** The purpose of this investigation is therefore, to study the relationship of physical activity and body habitus with prostate cancer mortality among Puerto Rican men. This study uses an observational longitudinal design with a random sample of 9,824 Puerto Rican men aged 35-79 years at baseline (1964) who were part of the Puerto Rico Heart Health Program (PRHHP). The Puerto Rico Heart Health Program provides a unique epidemiological cohort of men who took part in multiple examinations including extensive information on lifestyle, diet, body composition, exercise, and smoking habits. Survival analyses will be used to study the relationship between prostate cancer mortality and physical inactivity and obesity with approximately 35 years of follow up data. **Scope of the research:** This research is to generate new knowledge of how sedentary lifestyles or excess body weight are related to prostate cancer mortality, and to increase our knowledge of prostate cancer in a population where prostate cancer is the number one killer. Additionally, once prostate cancer mortality is identified, other exposures such as diet, smoking and alcohol intake can also be studied.

BODY:

Below is an itemized list of activities that have been conducted during the past year of the research and our progress in completing these tasks. Primarily we have published several manuscripts addressing the relationship of inactivity, obesity, and prostate cancer risk. We have also presented multiple abstracts with our preliminary results on these associations and providing the background for further publications. We identified other dietary components that may be related to prostate cancer to further understand this part of the energy balance component. The manuscript examining diet and prostate cancer was accepted in *Nutrition and Cancer*. The manuscript Physical activity and prostate cancer mortality: results from the Puerto Rico Heart Health Program has been submitted to the *International Journal of Cancer*. The manuscripts on "Body mass index and its relationship to prostate cancer mortality in US Whites and Blacks: the feasibility J-shaped curve" was submitted to the *American Journal of Epidemiology*, but was not accepted for publication. We have incorporated suggestions from the reviewers and will be submitting to a second journal.

While we are presenting some tables and figures in the body of the report, the reviewers can find a comprehensive discussion of the findings in the appended manuscripts. We found a null relationship between physical activity and prostate cancer, while the association between BMI and prostate cancer seems to be J-shaped.

We encountered some problems in accomplishing some of our tasks. From our report in year 02 we further validated our prostate cancer mortality cases and found that the total number of prostate cancer cases went up from 74 to 88. The increase is explained by further validating ICD codes in the databases and by purchasing the death certificates of the cases. The 74 prostate cancer cases where those with ICD-9 and excluded prostate cancer cases with ICD-10. Our revised estimates include ICD-9 and ICD-10 prostate cancer cases. During the past two years we have been working very closely with the Puerto Rico Cancer Registry to update our prostate cancer mortality cases. This resulted in a delay to submit this report, but we are now more confident of the added statistical power with more prostate cancer cases. We carefully analyzed our data to look at body weight, weight gain, and relative body weight as they relate to prostate cancer mortality.

Manuscript 1:

In our manuscript examining the relationship between physical activity and prostate cancer we found no relationship between quartiles of physical activity, participation in vigorous physical activity and engaging in no physical activity for 12 or more hours a day. We found that none of these physical activity measures were related to prostate cancer mortality. Table 1 lists the distribution of prostate cancer mortality cases and non-cases.

Table 1. Baseline Characteristics of the Puerto Rico Heart Health Program participants according to prostate cancer mortality.

	Prostate Cancer Deaths (n=167)		Non Cases (n=9613)		Chi-square P-value
	n	%	n	%	
Age, years					0.04
35-44	3	1.8	345	3.6	
45-54	69	41.3	4840	50.4	
55-64	82	49.1	3763	39.2	
65+	13	7.8	665	6.9	
Education					0.09
No formal schooling	16	9.6	975	10.1	
Grades 1-4	51	30.5	3392	35.3	
Grades 5-8	58	34.7	2754	28.7	
Attended/completed high school	22	13.2	1700	17.7	
More than high school	20	12.0	786	8.2	
Living					0.52
Urban	47	28.1	2928	30.5	
Rural	120	71.9	6685	69.5	
Smoking					0.53
None	51	30.5	3237	33.7	
Past	73	43.7	4208	43.8	
Current	43	25.8	2159	22.5	
BMI (weight (kg) / height $(m)^2$)					0.89
Underweight (<18.5)	4	2.4	310	3.2	
Normal weight (18.5-24.9)	76	45.5	4530	47.1	
Overweight (25-29.9)	66	39.5	3609	37.5	
Obese (30+)	21	12.6	1164	12.1	
Physical activity					0.64
Quartile 1 (low)	43	25.8	2621	27.3	
Quartile 2	38	22.8	2381	24.8	
Quartile 3	46	27.5	2240	23.3	
Quartile 4 (high)	40	24.0	2371	24.7	

We found no relationship between physical activity and prostate cancer mortality. Quartile 1 includes the most inactive category at baseline. More active groups did not have significantly lower or higher risk of prostate cancer mortality. Adjustment for other confounders did not alter this relationship. Participation in vigorous leisure time physical activity 1 hour or more a day, was also not protective against prostate cancer.

To further study the types of physical activity associated with fatal prostate cancer mortality we examined the relationship of vigorous physical activity with prostate cancer risk. Table 2 shows the relationship according to vigorous physical activity among overweight participants (BMI>=25) and older men (55 yrs and older).

Table 2. Odds Ratios for prostate cancer mortality in relation to baseline physical activity (167 cases among 9613 men).

	Quartiles of Physical Activity			
	Q1	Q2	Q3	Q4
Overall				
Range				
OR (95% CI)[a]	1.0	1.01 (0.65-1.58)	1.32 (0.87-2.02)	1.10 (0.71-1.71)
OR (95% CI)[b]	1.0	0.99 (0.64-1.55)	1.34 (0.88-2.05)	1.19 (0.75-1.90)
BMI: underweight or normal weight				
OR (95% CI)[c]	1.0	1.22 (0.62-2.41)	1.64 (0.87-3.09)	1.07 (0.55-2.11)
BMI: overweight or obese				
OR (95% CI)[c]	1.0	0.87 (0.49-1.56)	1.22 (0.68-2.18)	1.53 (0.81-2.91)
Age: <55 years				
OR (95% CI)[d]	1.0	1.35 (0.67-2.73)	1.63 (0.82-3.24)	1.03 (0.47-2.25)
Age: 55+ years				
OR (95% CI)[d]	1.0	0.78 (0.43-1.41)	1.20 (0.69-2.09)	1.34 (0.75-2.38)

[a] adjusted for age (35-44, 45-54, 55-64, 65+ years) and BMI (underweight, normal weight, overweight, obese)
[b] adjusted for age, education (no formal schooling, grades 1-4, grades 5-8, attended/completed high school, more than high school), BMI, living (urban, rural), and smoking (never smoker, current smoker, past smoker)
[c] adjusted for age (continuous years), education, living, and smoking
[d] adjusted for age (continuous years), education, BMI, living, and smoking

Innovative Minds in Prostate Cancer Today (IMPaCT) Abstract:

Using data from the Puerto Rico Heart Health Program we analyzed our results based on established body mass index categories. Table 3 shows the risk of mortality from prostate cancer according to baseline overweight classification.

Table 3. Age-adjusted odds ratios of the relationship between overweight and obesity classification and risk of fatal prostate cancer among Puerto Rican men.

	Cases	Odds Ratios	95% Confidence Interval	P-value
Underweight BMI<18.5	4	0.70	0.25, 1.93	0.499
Healthy weight BMI=18.5-24.9	76	1.0	Reference	
Overweight BMI= 25-29.9	66	1.11	0.79, 1.55	0.548
Obese BMI>=30	21	1.10	0.67, 1.79	0.707

Our results indicate that existing body mass classification do not explain an excess prostate cancer mortality associated with obesity or excess body weight.

Manuscript 2:

To better understand the relationship between BMI and prostate cancer, we therefore examined another dataset with a large number of prostate cancer cases that included minority populations from the National Health Interview Survey (NHIS). We were able to examine a J-shaped correlation matrix between BMI and prostate cancer among Whites and Blacks. The NHIS is a national representative sample of the US population conducted by the Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics. Participants are sampled yearly and follow up with mortality using the National Death Index within the CDC. Table 1 is a descriptive characterization of US Blacks and Whites that we used as our analytic sample obtained from the National Health Interview Survey.

Table 4. Number, Average BMI, Average Income, and Average Education by Race and age groups for Prostate Deaths, Other Deaths, and the Living

	Prostate Deaths				Other Deaths				Living			
	No.	BMI	Income	Educ	No.	BMI	Income	Educ	No.	BMI	Income	Educ
Blacks												
40 – 49	1	32.4	.	12	399	26.9	22811	11.3	6082	26.7	31748	12.2
50 – 59	20	28.5	22742	10.3	604	26.5	22724	10.1	4107	27.1	29842	11
60 – 69	62	26.6	19039	9.8	1003	25.9	17926	8.8	3037	26.7	22309	9.7
70 – 79	77	26.2	15511	7.5	847	25	14821	7.8	1378	26	16866	8.6
80 +	35	24.1	14716	6.8	438	24.1	12305	6.3	313	24.6	13323	6.8
Whites												
40 – 49	11	27.9	42136	13.4	1337	26.9	35086	12.5	44712	26.6	43223	13.7
50 – 59	24	26.5	44048	12.8	2631	26.6	33621	11.8	30503	26.8	42278	13
60 – 69	166	26.7	33686	11.8	5472	26	27213	11.4	24117	26.4	33235	12.3
70 – 79	287	25.1	24804	11.4	6722	25.1	22486	10.8	12302	25.6	25964	11.6
80 +	167	23.7	20676	10.1	3912	23.6	20736	10.1	2697	24.6	22359	10.8

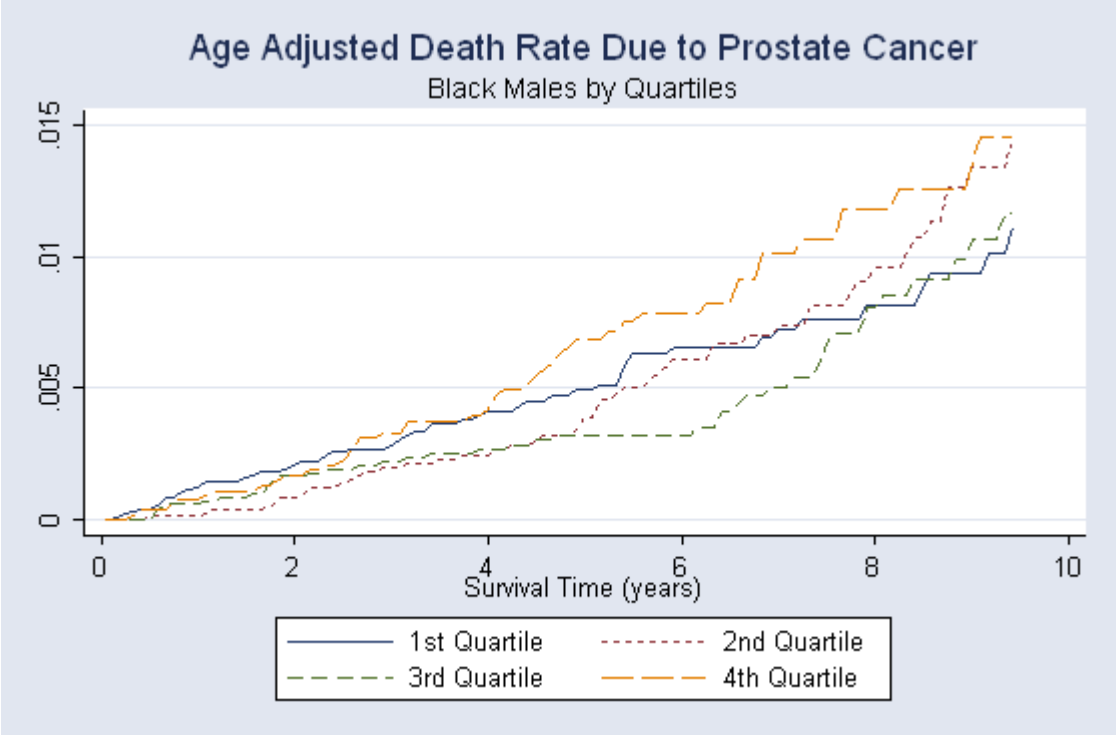

Figure 1

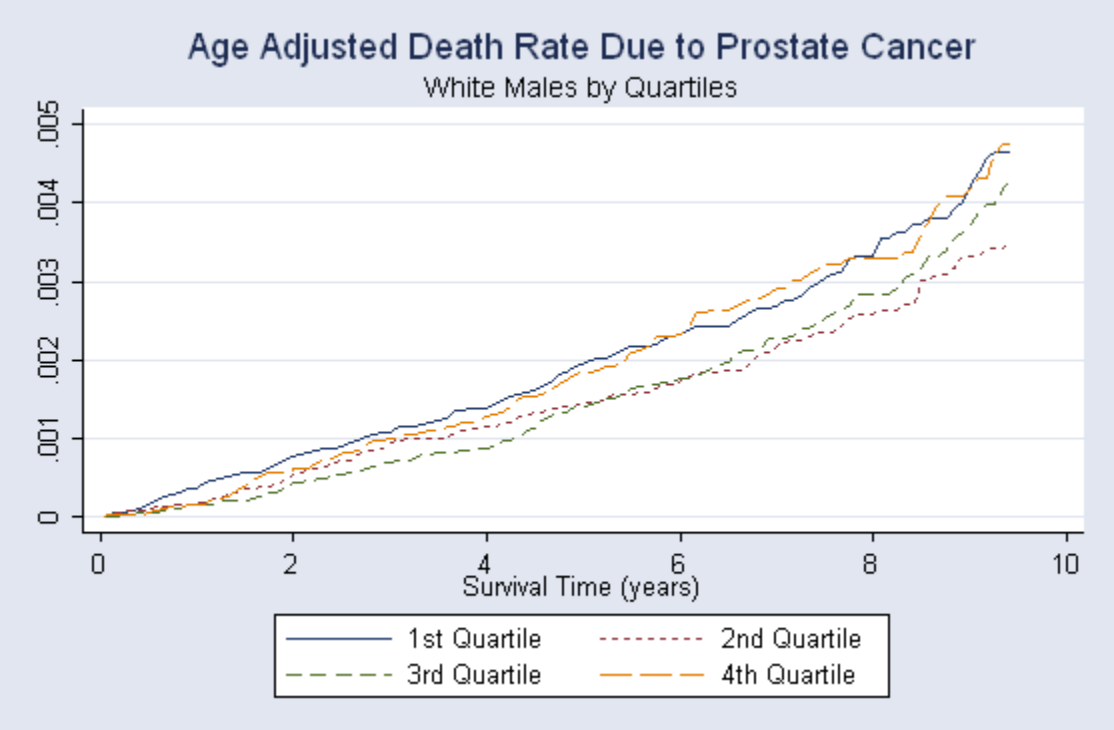

Figure 2

Figures 1 and 2 above show a survival curve of prostate cancer mortality according to different BMI quartiles among Blacks and Whites using a national representative sample dataset from the National Health Interview Survey.

Key research accomplishments:

1. Our results show that physical activity is not related to prostate cancer mortality in this group of Puerto Rican men. This is consistent with findings from other longitudinal studies. However, other studies have found it to be protective.
2. Analysis of body mass index classification showed no excess prostate cancer mortality associated with obesity or overweight status.
3. We applied a Cox proportional hazard modeling to assess the possibility that the relationship between BMI and prostate cancer is J-shaped rather than linear. Our findings showed significant increases in fatal prostate cancer mortality for Whites and Blacks.
4. Our manuscript on physical activity and prostate cancer in Puerto Rican men will be the first paper to assess prostate cancer mortality among Hispanics.
5. The manuscript on BMI and prostate cancer mortality is the first paper to attempt to fit a J-shaped curve in a White and Black population.
6. We published a paper in the *British Journal of Urology*, titled "Association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms in older American men: findings from the NHANES III." (Br J Urol. 2005 Jul;96(1):77-82). Lower Urinary Tract Symptoms (LUTS) has been associated with prostate hyperplasia and prostate cancer. We examined the cross sectional relationship of lifestyle factors, including physical activity and LUTS in Black, White and Hispanic men from the National Health and Nutrition Examination Survey – see appendix. (1)
7. We published a paper to examine pulse pressure as an independent risk factor for cardiovascular disease – see appendix (2). We propose to assess how pulse pressure, which is a surrogate of cardiovascular stiffness, relates to prostate cancer mortality as has been reported by others (3-5). Moreover, we are proposing to further study the role fasting blood glucose or diabetes play in predicting prostate cancer risk given the identified protective associations in some populations, but not in others (6-8). According to the Centers for Disease Control and Prevention the prevalence of and mortality from diabetes is highest in the commonwealth of Puerto Rico compared with any other State in the Union. Thus, further investigation of the association of diabetes and prostate cancer will be of high public health significance.
8. Because African Americans have been reported to have one of the highest rates of prostate cancer mortality in the world we investigated the association of skin color among Puerto Rican men with all cause mortality. We were able to characterize the skin color variable among Puerto Rican men, and in the near future plan to examine the role that skin color plays in predicting prostate cancer mortality. Our initial findings indicate that skin color is not a risk factor for excess all cause mortality in this group of Puerto Rican men. This paper was accepted in *Annals of Epidemiology*.

9. Since body weight is related to diet and physical activity we examined the role that dietary components may have on predicting prostate cancer mortality. We examined the role of energy intake and selected dietary components with prostate cancer mortality. We studied the role of legume intake as a predictor of prostate cancer and found no association. This was important as other researchers have found soy beans to play a protective role. There have been few studies that have looked at other non-soy legumes. Legume intake was not associated with prostate cancer mortality (comparing highest quartile to lowest quartile: 1.40 (95% CI 0.91-2.18), p-trend 0.17), nor were total protein, animal, seafood, dairy, or vegetable protein intakes. Consuming 1-2 servings of fruit was inversely associated (OR 0.50, 95% CI 0.32-0.77), whereas consuming more than 2 servings of fruit was not associated with prostate cancer mortality. Thus, we find no association between legumes or protein intake and prostate cancer mortality in this longitudinal cohort study of Puerto Rican men. This paper was accepted in *Nutrition and Cancer*.

Reportable outcomes:

Manuscripts:
We have four articles that have been published, accepted for publication, or submitted.

1. Smit E, Garcia-Palmieri MR, Figueroa NR, McGee DL, Messina M, Freudenheim JL, Crespo CJ. Protein and legume intake and prostate cancer mortality in Puerto Rican men. Nutrition and Cancer, In Press.
2. Borrell L; Crespo CJ, Garcia-Palmieri MR. Skin color and mortality risk among men: The Puerto Rico Heart Health Program. Annals of Epidemiology. In Press
3. Rohrman S, Giovanucci E, Smit E, Crespo CJ, Platz E. Association of Cigarette Smoking, Alcohol Consumption, and Physical Activity With Lower Urinary Tract Symptoms in Older US Men in the Third National Health and Nutrition Examination Survey (NHANES III). British Journal of Urology. 2005;96:77-82.
4. Crespo CJ, Physical activity in minority populations: Overcoming a public health challenge. President's Council on Physical Fitness and Sports. Research Digest, Series 6, No. 2, June 2005.
5. Garcia-Palmieri MR, Crespo CJ, McGee DL, Smit E, Sempos CT, and Sorlie PD. Wide pulse pressure as a risk factor for cardiovascular mortality. Results from the Puerto Rico Heart Health Program. Nutrition Metabolism and Cardiovascular Disease. 2005;15:71-78.
6. CrespoCJ, Smit E, Fuhrman B, Figueroa Valles N, Ramirez-Marrero FA, McGee D, Garcia-Palmieri M. Physical activity and prostate cancer in Puerto Rican men. Submitted.
7. McGee DL, Crespo CJ, McGee D. The relationship of BMI and prostate cancer mortality in Black and White men: Results from the National Health Interview Survey Mortality follow up. Submitted.

Abstracts:

1. **Crespo CJ,** Fuhrman B, Smit E, Freudenheim J, Zayas L, Ramirez-Marrero F, McGee D, Garcia Palmieri M, Urban Living and Risk of Fatal Prostate Cancer among Puerto Rican Men: The Puerto Rico Heart Health Program. North American Congress of Epidemiology, June, 2006.
2. Fuhrman B, Smit E, Freudenheim J, Zayas L, Ramirez-Marrero F, McGee D, Garcia Palmieri M, **Crespo CJ.** Coffee Intake and Risk of Incident Diabetes in the Puerto Rico Heart Health Stuidy Cohort. North American Congress of Epidemiology, June, 2006.
3. Burrell L, **Crespo CJ**, Skin color and mortality risk among men: The Puerto Rico Heart Health Program. North American Congress of Epidemiology, June, 2006.
4. **Crespo CJ**, Fuhrman B, Smit E, Freudenheim J, Garcia Palmieri M, Muti P, Fasting glucose and prostate cancer mortality among Puerto Rican men. American Association for Cancer Research. Frontiers in Cancer Prevention, September, 2005, Baltimore, MD
5. **Crespo CJ**, Garcia-Palmieri M, Smit E, McGee D, Lee IM, Balderrama F, Sorlie P. Physical activity is not protective against prostate cancer mortality among Puerto Rican men. American College of Sports Medicine, June, 2005, Nashville, TN, Medicine and Science in Sports and Exercise, 2005;37: Supplement. Abstract
6. E Smit, TM Brasky, FA Ramirez-Marrero, N Valle-Figueroa, JL Freudenheim, MR Garcia-Palmieri, **CJ Crespo**. Legume and protein intake and prostate cancer mortality in Puerto Rican men, Society for Epidemiology Research. June 2005, Toronto, Canada
7. **Crespo CJ**, Ramirez FA, Nazario CM, Fernandez N, Marshall J, Michalek A. Collaborative Cancer Research in Puerto Rico: Setting the research agenda. Second Puerto Rican Public Health Conference, San Juan, PR, September 1-3, 2004.

Conclusions:

Importance of completed research:

The importance of the completed research is that our findings support the hypothesis that physical activity is not related to prostate cancer. While the relationship between physical activity and prostate cancer remains inconclusive, our research lends evidence of a null relationship. Moreover, recent investigations have linked increased obesity with prostate cancer while other studies – including ours – suggest that excess body weight is not related to prostate cancer. Our results further support this null finding; however, in examining the J-shape relationship between BMI and prostate cancer we may be able to highlight the fact that body weight relationship with prostate cancer is not linear.

Changes on future work:

Our study on the relationship of body habitus and prostate cancer shows that BMI is not linearly related to prostate cancer mortality. Our findings are the first one to examine a J-shaped relationship, in both Whites and Blacks. Therefore, future work - and already published studies – should carefully examine whether a J-shaped curved is a better predictor of prostate cancer mortality. We are also proposing to examine the

relationship of skin color with prostate cancer. While it is clear that African American have one of the highest rates of prostate cancer mortality in the world, it is not easy to find populations with similar environment but of different skin colors. In the PRHHP, skin color was measured at the upper inner arm (with low sun exposure) using color tiles and participants were classified based on the von Luschan scale. These color tiles were used by an anthropologist at the time of the study and consisted of 30 colored tiles representing shades of skin color from very light to very dark. The color tiles were matched to each participant's skin color. While we found that skin color was not related to all-cause mortality, it is not clear if skin color is related to prostate cancer mortality.

So what section:

While our results showed that physical activity is not related to prostate cancer mortality other studies have found an inverse relationship. Even when we limit the evidence to longitudinal studies, the findings remain inconclusive. Future studies, therefore, should aim at better characterizing physical activity into primarily aerobic or anaerobic. The effect of aerobic or anaerobic physical activities on circulating testosterone may provide additional insights on how exercise relates to prostate cancer.

Additionally, our original analysis on the relationship between BMI and prostate cancer in Puerto Rican men showed no significant relationship. In order to have a larger sample size to assess other types of relationships, we studied data from the National Health Interview Survey which contain over 600 prostate cancer cases and also had a substantial number of Whites and Blacks. With a larger number of cases we were able to test the hypothesis that the relationship between BMI and prostate cancer was not linear but that a J-shaped curve was a better predictor of prostate cancer mortality. Thus, future studies – and already published studies - should attempt to model this J-shaped relationship to better characterize the role of BMI on prostate cancer risk. Moreover, this new finding could provide some evidence of a minimum and maximum threshold for which a BMI level may increase the risk for prostate cancer.

Reference List

(1) Rohrmann S, Crespo CJ, Weber JR, Smit E, Giovannucci E, Platz EA. Association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms in older American men: findings from the third National Health And Nutrition Examination Survey. *BJU Int* 2005; 96(1):77-82.

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(3) Ronquist G, Rodriguez LA, Ruigomez A, Johansson S, Wallander MA, Frithz G et al. Association between captopril, other antihypertensive drugs and risk of prostate cancer. *Prostate* 2004; 58(1):50-56.

(4) Dockery F, Bulpitt CJ, Agarwal S, Donaldson M, Rajkumar C. Testosterone suppression in men with prostate cancer leads to an increase in arterial stiffness and hyperinsulinaemia. *Clin Sci (Lond)* 2003; 104(2):195-201.

(5) Fitzpatrick AL, Daling JR, Furberg CD, Kronmal RA, Weissfeld JL. Hypertension, heart rate, use of antihypertensives, and incident prostate cancer. *Ann Epidemiol* 2001; 11(8):534-542.

(6) Kasper JS, Giovannucci E. A meta-analysis of diabetes mellitus and the risk of prostate cancer. *Cancer Epidemiol Biomarkers Prev* 2006; 15(11):2056-2062.

(7) Gong Z, Neuhouser ML, Goodman PJ, Albanes D, Chi C, Hsing AW et al. Obesity, diabetes, and risk of prostate cancer: results from the prostate cancer prevention trial. *Cancer Epidemiol Biomarkers Prev* 2006; 15(10):1977-1983.

(8) Tavani A, Gallus S, Bertuzzi M, Dal ML, Zucchetto A, Negri E et al. Diabetes mellitus and the risk of prostate cancer in Italy. *Eur Urol* 2005; 47(3):313-317.

Appendices:

1. Physical activity and prostate cancer mortality in Puerto Rican Men
2. Protein and legume intake and prostate cancer mortality in Puerto Rican men
3. Skin color and mortality risk among men: The Puerto Rico Heart Health Program
4. Association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms in older American men: findings from the NHANES III
5. Revised draft of paper on BMI and prostate cancer mortality in Black and White men.
6. Abstracts:
    a. Obesity as a predictor of prostate cancer mortality in Puerto Rican men
    b. Urban Living and Risk of Fatal Prostate Cancer among Puerto Rican Men: The Puerto Rico Heart Health Program

Physical activity and prostate cancer mortality: results from the Puerto Rico Heart Health Program.

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Acknowledgement:

This work was supported by the following grant: DAMD17-02-1-0252

Introduction:

Second to lung cancer, prostate cancer kills more men than any other cancer in the United States. A large number of deaths from prostate cancer is also observed among other Western societies (1;2). Although microscopic (latent) prostate tumors in most populations are similar, striking differences in the incidence rates among racial/ethnic groups exist (2;3). The incidence and mortality from cancer among African American men is considered one of the highest in the world (4;5). During the years of 1988 and 1992, the highest reported rates (age-adjusted world standard), exceeding 30,000 per 100,000 man years, were observed among US blacks. Rates in Black Caribbean men, especially from Jamaica, are also among the highest in the world. Prostate cancer mortality among all Hispanics in the US are considered lower than those of non-Hispanic whites, however, differences among Hispanic subgroups support an increased burden of prostate cancer mortality among Puerto Ricans and other Caribbean men of different skin color (6-9).

Prostate cancer rates in the Commonwealth of Puerto Rico are not very dissimilar to those observed in the United States. For example, the age-adjusted prostate cancer mortality rates among men from Puerto Rico and the United States are 16.1/100,000 and 15.7/100,000 respectively. However, prostate cancer kills more Puerto Rican men in Puerto Rico than any other cancer, including lung cancer. Puerto Ricans in the United States are the second largest Hispanic subgroup and have prostate cancer mortality rates lower than those observed in Puerto Rico, but higher than other Hispanic subgroups such as Mexican Americans or Cuban Americans(10-13). The fact that prostate cancer rates change in migrant populations and vary dramatically in ethnically similar populations

residing in different geographic locations strongly suggest that environmental factors can greatly influence the risk of this cancer (14). Despite the large number of deaths from prostate cancer among men and minority men, there is little knowledge about lifestyle changes that can modify the risk. (4;10-13;15-24)

One important lifestyle that has been associated with prostate cancer is physical activity. The relationship between physical activity and prostate is not consistent across studies. While some studies show a small protective benefit, there are several reports showing no relationship or an increased risk with physical activity. Moreover, the relationship between physical activity and prostate cancer among US Hispanic men has not been well characterized (25-38). The purpose of this study is to examine the relationship between physical activity and prostate cancer mortality in a cohort of Puerto Rican men who took part in the Puerto Rico Heart Health Program.

Methods:

Study population:

The Puerto Rico Heart Health Program is a prospective cohort study designed to examine morbidity and mortality from coronary heart disease in urban and rural Puerto Rican men (39-42). Briefly, the original sampling was designed to recruit men aged 45 to 64 years who were free from coronary heart disease at time of first examination in 1965. These men were sampled from 3 urban areas and 4 rural areas in the northeast part of Puerto Rico by the personnel who participated in the United States decennial census (40). All of these men were encouraged to attend the baseline examination, and an 80% response rate was achieved. The original sample of the cohort consisted of men ages 45

to 64 years of age. Other participants aged 35-44 years and 65 to 79 years, who were not part of the original sampling frame were also included in the present study. Thus, the total number of examined participants used in this analysis includes 9,824 men between the ages of 35 to 79 years.

All men completed an extensive self-report of demographic characteristics, personal and family health history, and health habits, including education, occupation, income, a history of smoking, and place of residence among other characteristics.

Assessment of physical activity and other characteristics:

During the first examination each participant provided sociodemographic information and a complete medical history with a physical examination that included laboratory determination, and a resting 12-lead electrocardiogram was conducted. At this first examination, physical activity status was assessed using the Framingham Physical Activity Index (41;43). This questionnaire assesses occupational, leisure-time and other physical activities, measured as usual activity over the course of a 24-hour day and was interviewer-administered. Usual physical activity was determined by a review of the number of hours spent at various activities. For analysis, the number of hours at each activity was converted to an index of usual daily energy expenditure. This was accomplished by grading activities into different categories using estimated oxygen consumption per hour for each activity or metabolic equivalents (METs). One MET is equivalent to energy expenditure at rest, approximately 3.5 ml of O_2 per kilogram of body weight per minute. The usual activities were classified using the original scheme used in the Framingham Study as sedentary (MET=1.0), light (MET=1.1-2.3), lightly moderate

to moderate (MET=2.4-4.9) and strenuous (MET=5.0+). The product of this grade and duration in hours gave a score of a physical activity index. A score of 24 meant the individual slept or reclined for 24 hours in a day. Higher scores indicated either strenuous activity for shorter periods and/or moderate activity for a longer time. Estimates of consistency of administration between the first test using the Framingham Physical Activity Index and 2- to 3-year post-test in this group of Puerto Rico men provided Pearson correlation coefficients of .30 to .59 (41;44).

We categorized our analytic sample by quartiles of physical activity. The physical activity index ranged from 24 to 71. We further examined patterns of physical activity within quartile by hours spent doing no activity such as sleeping or resting; sedentary or very light activities such as sitting; light activities such as walking at level; moderate physical activity such as brisk walking, climbing stairs or walking uphill; and vigorous physical activity such as cutting sugar cane or other strenuous activities. The cutoff point for quartile 1 was a physical activity index of 27 or less and represents the group that is most inactive. To assure quartile 1 reflects only those who are sedentary, we reclassified 18 participants (out of 2401) from quartile 1 into quartile 2 (N=2277). These participants had a physical activity index of less than 27 but reported participating in some type of moderate physical activities. Thus, quartile 1 of physical activity includes participants who only engaged in no physical activities, sedentary activities or very light physical activities. The range of physical activity index for quartile 2 was greater than 27 but less than 30, for quartile 3 the range was greater than or equal to 30 but less than 37 (N=2171), and for quartile 4 scores were greater than or equal to 37 (N=2287).

Obesity classification:

We used the guidelines released by the National Heart, Lung, and Blood Institute; National Obesity Education Initiative to classify our participants based on body mass index (BMI) (45). Briefly, underweight individuals are those whose BMI was less than 18.5; normal or healthy weight represent persons with BMI between 18.5 and 24.9; overweight are persons with BMI between 25 and 29.9; and obese are persons with a BMI of 30 and above.

Other covariates:

Education level was determined from the interview by ascertaining the highest grade completed in school. For our analysis, participants were grouped into five categories: No formal schooling, and those who attended or completed grades 1-4, grades 5-8, high school, or college. The detailed smoking history provided the basis to classify participants into nonsmokers, previous smokers, and smokers. Rural-urban residence was determined based on place of residence at baseline. Characterization of rural areas was composed primarily of small farms located on very hilly terrain while urban areas consisted of a denser cluster of houses, many of whose residents worked in the business and industry around San Juan.

Ascertainment of fatal prostate cancer:

Prostate cancer mortality was assessed throughout the active phase of the study and 35 men had died of prostate cancer by 1980. An additional 88 prostate cancer deaths

between 1981 and 2002 were ascertained using passive follow-up by matching participants in the Puerto Rico Heart Health Program with the Puerto Rico Cancer Registry and Puerto Rico Vital Statistics Registry. Cases were matched on the basis of a full match with first name, maternal and paternal last names, date of birth, place of birth, and gender. Validity of matched cases was assessed by obtaining copies of the death certificate. A recent update (2003-2005) from the Puerto Rico Cancer Registry identified an additional 44 prostate cancer deaths. In total, there were 167 prostate cancer deaths in the study population.

Statistical Analysis:

The outcome variable of interest was mortality from prostate cancer. The multivariate logistic function model was used to analyze relationships between known risk factors and prostate cancer mortality. We examined the potential contribution of the following variables in the model: age (years), education (no formal schooling, grades 1-4, grades 5-8, attended or completed high school, attended or completed college), body weight classification (underweight, healthy weight, overweight, obesity), baseline smoking status (non-smokers, former smokers, current smokers), and urban-rural residence (urban, rural) (43;46-48).

Results:

The analytic sample consisted of 9780 participants with complete data (44 of the 9824 men who participated in the PRHHP study had missing or incomplete data on physical activity). Prostate cancer deaths will be referred to as cases and the remainder of

the cohort will be referred to as non-cases. Selected baseline characteristics of the study population are shown in table 1. Cases were older and somewhat more educated than non-cases. Smoking, body mass index, and physical activity were similar between cases and non-cases. The percent distribution in different quartiles of physical activity ranged from 22.8 percent to 27.5 percent, showing little variability both among cases and non-cases.

Insert Table 1 Here

After adjustment for age and BMI, we found that physical activity was not associated with prostate cancer mortality in this group of Puerto Rican men. Adjustments for other confounders outlined in Table 1 did not modify the relationship; these other confounders were not significantly related to prostate cancer either.

Insert Table 2 Here

To better understand if the relationship of physical activity differed by categories of body mass index and age we stratified our cohort among those who were overweight or obese (BMI>=25) and those who were not overweight (BMI<25). After stratifying by these two BMI categories, physical activity was not a predictor of physical activity either. Similarly, stratifying the cohort among those who were younger than 55 years of age at baseline and among those who were 55 years of age or older showed that physical activity was not a predictor of prostate cancer mortality.

We further examined the role that participation in vigorous physical activity may have in predicting prostate cancer mortality. Participants in the cohort were grouped

based on their baseline participation in vigorous physical activity (MET>=5) for one hour or more a day. The age-adjusted odd ratios among those reporting participating in vigorous physical activity for 1 or more hour a day was 0.96 (95% CI = 0.68, 1.34). Adjustment for education, body mass index and smoking did not alter the results significantly. Stratifying the analysis among those younger than 55 years of age (OR=0.70; 95% CI=0.456, 1.21) or 55 years or older (OR=1.17; 95% CI=0.76, 1.80) did not yield a significant relationship between vigorous physical activity and fatal prostate cancer. Thus, in this cohort of men participation in vigorous physical activity for 1 or more hours did not confer any significant protection against prostate cancer mortality.

Discussion

In our review of the literature we found that the relationship between physical activity and prostate cancer risk across studies was not consistent. While some longitudinal studies have found a protective effect of physical activity on prostate cancer risk (28;34;38;49-56), other longitudinal studies found no association or positive association between physical activity and prostate cancer (31;35;37;57-62). It is not surprising the several comprehensive reviews of the literature that included longitudinal and case-control studies concluded that the relationship between physical activity and prostate cancer remains inconsistent (32;63). Our results are in accordance with those that found no association between physical activity and prostate cancer. We did not observe a dose-response trend either and adjustment for age, BMI, smoking or education did not change the association.

The majority of the studies above were conducted in men of European ancestry. One study was from Shanghai, another from Hawaii, and another had data on African Americans (49;50;64). Severson et al (55) used the same physical activity index from the Framingham study and heart rate (as a marker of physical fitness) in a cohort of 7,925 Japanese men in Hawaii aged 46-65 years to examine their associations with prostate cancer incidence. After adjustment for age and BMI they found no association when comparing the most active relative to the least active men, no protective effect of occupational physical activity, and heart rate was not related to prostate cancer incidence either. Our findings are the first longitudinal study of physical activity and prostate cancer in a large group of Hispanics men.

In our study we focused on prostate cancer mortality and not incidence. Prostate cancer mortality may be a reflection of the most aggressive prostate cancer cases, and therefore is of great public health significance. By using fatal prostate cancer we also avoid the possibility of increase prostate cancer incidence due to secular trends in higher incidence due to screening. Active men may be more likely to undergo screening and may have higher rates of incidence prostate cancer especially at early stage. By concentrating our efforts on prostate cancer mortality we reduce this bias. Prostate cancer ascertainment was conducted in conjunction between the Puerto Rico Cancer Registry and the Puerto Rico Office of Vital Statistics. The Puerto Rico Cancer Registry is a full member of the North American Association of Central Cancer Registry and adheres to Data Standards for Cancer Registry established by this organization. Our reliance on prostate cancer mortality allowed us to also validate our mortality cases by obtaining death certificates on a subset of 88 cases. Of these 88 requests for death

certificate we received 87 death certificates with prostate cancer mortality as the underlying cause of death. Thus, we believe our ascertainment of fatal prostate cancer using the two Registries is valid.

Our exposure variable physical activity has been used in other studies, however, on potential limitation of our study is that it may not be specific enough to differentiate lifetime or usual levels physical activity. This is not a unique problem of this study as objective measures of physical activity for use in large epidemiological studies are not yet feasible. We further studied participation in vigorous physical activity to examine if the intensity of participation in physical activity is important for prostate cancer. One hypothesis that changes in testosterone levels associated with participation in aerobic compared with anaerobic physical activity may have a differential effect on prostate cancer. Our findings failed to observe an association between vigorous physical activity and prostate cancer in contrast to results from Giovannucci et al., (2005) (36;38).

In summary physical inactivity was not a risk factor for fatal prostate cancer in this group of Puerto Rican men. While most of the literature that have reviewed the relationship between prostate cancer and physical activity have been among European whites, our study is the first to examine this relationship longitudinally in a well characterized subgroup of Hispanics. Further studies should examine the role of lifetime physical activity and incorporation of more valid objectives measures of physical activity to examine the role of physical activity in the prevention of prostate cancer.

Table 1. Baseline Characteristics of the Puerto Rico Heart Health Program participants according to prostate cancer mortality.

	Prostate Cancer Deaths (n=167)		Non Cases (n=9613)		Chi-square P-value
	n	%	n	%	
Age, years					0.04
35-44	3	1.8	345	3.6	
45-54	69	41.3	4840	50.4	
55-64	82	49.1	3763	39.2	
65+	13	7.8	665	6.9	
Education					0.09
No formal schooling	16	9.6	975	10.1	
Grades 1-4	51	30.5	3392	35.3	
Grades 5-8	58	34.7	2754	28.7	
Attended/completed high school	22	13.2	1700	17.7	
More than high school	20	12.0	786	8.2	
Living					0.52
Urban	47	28.1	2928	30.5	
Rural	120	71.9	6685	69.5	
Smoking					0.53
None	51	30.5	3237	33.7	
Past	73	43.7	4208	43.8	
Current	43	25.8	2159	22.5	
BMI (weight (kg) / height $(m)^2$)					0.89
Underweight (<18.5)	4	2.4	310	3.2	
Normal weight (18.5-24.9)	76	45.5	4530	47.1	
Overweight (25-29.9)	66	39.5	3609	37.5	
Obese (30+)	21	12.6	1164	12.1	
Physical activity					0.64
Quartile 1 (low)	43	25.8	2621	27.3	
Quartile 2	38	22.8	2381	24.8	
Quartile 3	46	27.5	2240	23.3	
Quartile 4 (high)	40	24.0	2371	24.7	

Note: in order to get p=trend I need to get medians for each quartile of the physical activity measure: need more info on the variable of phys act. Also present ranges for each quartile of the phys act.

Table 2. Odds Ratios for prostate cancer mortality in relation to baseline physical activity (167 cases among 9613 men).

	Quartiles of Physical Activity			
	Q1	Q2	Q3	Q4
Overall				
Range				
OR (95% CI)[a]	1.0	1.01 (0.65-1.58)	1.32 (0.87-2.02)	1.10 (0.71-1.71)
OR (95% CI)[b]	1.0	0.99 (0.64-1.55)	1.34 (0.88-2.05)	1.19 (0.75-1.90)
BMI: underweight or normal weight				
OR (95% CI)[c]	1.0	1.22 (0.62-2.41)	1.64 (0.87-3.09)	1.07 (0.55-2.11)
BMI: overweight or obese				
OR (95% CI)[c]	1.0	0.87 (0.49-1.56)	1.22 (0.68-2.18)	1.53 (0.81-2.91)
Age: <55 years				
OR (95% CI)[d]	1.0	1.35 (0.67-2.73)	1.63 (0.82-3.24)	1.03 (0.47-2.25)
Age: 55+ years				
OR (95% CI)[d]	1.0	0.78 (0.43-1.41)	1.20 (0.69-2.09)	1.34 (0.75-2.38)

[a] adjusted for age (35-44, 45-54, 55-64, 65+ years) and BMI (underweight, normal weight, overweight, obese)

[b] adjusted for age, education (no formal schooling, grades 1-4, grades 5-8, attended/completed highschool, more than highschool), BMI, living (urban, rural), and smoking (never smoker, current smoker, past smoker)

[c] adjusted for age (continuous years), education, living, and smoking

[c] adjusted for age (continuous years), education, BMI, living, and smoking

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Protein and legume intake and prostate cancer mortality in Puerto Rican men.

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Abstract

Prostate cancer is the number one cancer killer among Puerto Rican (PR) men. Plant foods have been inversely associated with prostate cancer. Legumes play a significant role in the PR diet; consumption of legumes in PR (14 pounds/capita) was double that of the U.S. (7 pounds/capita). We examined dietary protein consumption (from baseline 24 hour dietary recalls) and prostate cancer mortality in the PR Heart Health Program (PRHHP), a cohort study of 9,824 men aged 35-79 years at baseline (1964) with follow-up until 2005. Total protein intake in the cohort was 85 grams/day and sources of protein were: 30% vegetable, 30% dairy, 31% animal, and 8% seafood protein. Legume intake was 2.3 servings/day (1/4 cup each). Legume intake was not associated with prostate cancer mortality (comparing highest quartile to lowest quartile: 1.40 (95% CI 0.91-2.18), p-trend 0.17), nor were total protein, animal, seafood, dairy, or vegetable protein intakes. Consuming 1-2 servings of fruit was inversely associated (OR 0.50, 95% CI 0.32-0.77), whereas consuming more than 2 servings of fruit was not associated with prostate cancer mortality. Thus, we find no association between legumes or protein intake and prostate cancer mortality in this longitudinal cohort study of PR men.

Keywords: legumes, protein, prostate cancer mortality, Puerto Rico

Introduction

Puerto Ricans are the second largest group of Hispanics in the United States and have higher cancer mortality rates than all other Hispanic groups combined. Although prostate cancer mortality rates in Puerto Rico are similar to those observed in the United States, prostate cancer kills more men in Puerto Rico than any other cancer, including cancer of the lungs (1). Plant foods have been associated with a protection against prostate cancer in several epidemiological studies (2;3). More specifically, reduced prostate cancer risks have been associated with higher intakes of carotenoid-rich vegetables and soy products in Japan (4), higher intakes of beans, lentils, peas, and dried fruits among Seventh Day Adventist men (5), and higher tofu intake among Japanese men in Hawaii (6). Reduced mortality from prostate cancer has been also reported for men with higher intakes of cereals (7;8).

Legumes include peas, beans, lentils, and peanuts, and are a rich source of protein and dietary fiber. Beans and peas are staple foods of the Puerto Rican diet, particularly, pinto, kidney, small white, black-eye and black beans, and green pigeon peas and chick-peas (9;10). Consumption of legumes in Puerto Rico (14 pounds/capita)(11) is double that of the US (7 pounds/capita)(12).

There is interest in the role that legumes may play in reducing cancer risk, but the relationship between prostate cancer and legumes is not well-established (3;13-15). In a small case control study (n=60), Strom et al found that higher phytoestrogen intake was associated with a lowered risk of prostate cancer, but overall phytoestrogen intake was quite modest among the subjects in this study (16). In a meta-analysis of case-control studies in Canada, Jain et al reported reduced risks of prostate cancer associated with intake of beans, lentils and nuts (3). In a multi-center case control study that included African-Americans, whites, Japanese and Chinese populations from the U.S. and Canada, the relationship between prostate cancer risk and intake from soy and

non-soy legumes were studied separately. An inverse association between prostate cancer risk and non-soy legumes was found for African Americans, but not for whites, Japanese, or Chinese. However, soy foods were not significantly related to prostate cancer risk for any of the groups studied. Combining all legumes into one category yielded significant protection against prostate cancer for African Americans and Chinese men, but not for white or Japanese men (15).

Few studies have been able to study prospectively the relationship of diet with prostate cancer mortality among Hispanics. The aim of this study was to examine the relationship of dietary consumption of protein and legumes with prostate cancer mortality in Puerto Rican men.

Methods

The Puerto Rico Heart Health Program (PRHHP) is a prospective cohort study designed to examine morbidity and mortality from coronary heart disease (CHD) in urban and rural Puerto Rican men (17-19). In 1965, Puerto Rican men aged 45 to 64 years and who were free from CHD at time of first examination were recruited. Subjects were sampled from 3 urban areas and 4 rural areas in the northeast part of Puerto Rico by the personnel who participated in the U.S. decennial census (20). All of these men were encouraged to attend the baseline examination, and an 80% response rate was achieved. The original sample of the cohort consisted of men ages 45 to 64 years of age. Other participants whose age was not within this range (i.e., ages 35–44 years and 65 to 79 years of age), but who had been unintentionally included in the enumeration, were also included in this study. The total number of examined participants used in this analysis included 9,824 men between the ages of 35 to 79 years.

The baseline exam was conducted during the years 1965-1968. There were three subsequent exams, which took place during the years 1968-71, 1971-75, and

1974-77. Currently, active follow-up data are available for vital status and cause of death for the twelve-year period subsequent to a participant's initial examination date for 9,815 men; nine men were lost to follow-up over the twelve-year period. No cancer incidence data are available from the original study.

The design and methods used in the PRHHP were adapted from the Framingham Heart Study and validated by the U.S. National Institutes of Health for use in other population-based, observational, longitudinal cohorts such as the Honolulu Heart Study, the Israel Ischemic Heart Disease Project, and the Yugoslavia Cardiovascular Disease Study. During the baseline examination, all men completed an extensive self-report of demographic characteristics, personal and family health history, and health habits, including education, occupation, income, a history of smoking, and place of residence. Dietary intake was assessed using a 24 hour recall at baseline. Food models and standard-sized utensils were used to obtain a quantitative assessment from participants during a 24-hour dietary recall. Intake of energy and macronutrients was calculated using the United States Department of Agriculture Handbook #8 food composition tables or other more direct sources of nutrients analysis for foods special to Puerto Rico.

Prostate cancer mortality was assessed throughout the active phase of the study and 35 men had died of prostate cancer by 1980. An additional 88 prostate cancer deaths between 1981 and 2002 were ascertained using passive follow-up by matching participants in the Puerto Rico Heart Health Program with the Puerto Rico Cancer Registry and Puerto Rico Vital Statistics Registry. Cases were matched on the basis of a full match with first name, maternal and paternal last names, date of birth, place of birth, and gender. Validity of matched cases was assessed by obtaining copies of the death certificate. A recent update (2003-2005) from the Puerto Rico Cancer Registry

identified an additional 44 prostate cancer deaths. In total, there were 167 prostate cancer deaths in the study population.

Generalized linear regression models were used to obtain least square mean intakes and to adjust for confounding (i.e. age, education). Logistic regression models were used to obtain multivariate odds ratios (OR). Based on the distribution of the analytical cohort, the men were categorized into quartiles for each dietary intake measure, with the lowest quartile representing the referent category. Seafood protein (grams), seafood servings, and fruit intake, had high proportions of zero (no consumption) and thus were categorized as tertiles and binary variables as appropriate. Tests for trend were obtained by assigning the median value to each quantile of intake and treating it as a continuous variable. The residual method was used for energy adjustment (21). All statistical analyses were performed using SAS v9.1 software (Cary, NC).

Results

We examined the association of dietary intake with prostate cancer mortality in 167 prostate cancer deaths among 9777 men who participated in the PRHHP study and who had complete dietary intake data (47 of the 9824 men had missing or incomplete dietary intake data and were excluded). Prostate cancer deaths will be referred to as cases and the remainder of the cohort will be referred to as non-cases. Selected baseline characteristics of the study population are shown in table 1. Cases were older and somewhat more educated than non-cases. Smoking, body mass index, and physical activity were similar between cases and non-cases. Table 2 shows the mean intakes of macronutrients adjusted for age and education according to prostate cancer mortality. Total protein intake was 85 grams a day with 30% coming from vegetable sources, 30% from dairy, 31% from animal sources (such as beef, pork, and chicken)

and 8% from seafood. Macronutrient intake was similar between cases and non-cases. Additional adjustments for energy intake, physical activity, BMI, smoking and urban living did not significantly change the results.

The mean intake of legumes was 2.3 servings a day which is equivalent to approximately 5/8 cup per day and total vegetable intake including legumes was 5.1 servings a day for an equivalent of 1 ¼ cups a day. Meat consumption was approximately 3 oz a day. Dairy consumption (milk, cheese, and ice-cream) was 4.4 servings a day, and included 4.0 servings from milk for an equivalent of 2 cups (16 oz) of milk a day. Most of the milk intake came from coffee consumption as it is customary to drink 1 oz of coffee with about 4 oz of milk (22). Coffee consumption was approximately 3 oz and thus accounts for 12 oz of the total 16 oz of milk. Although legume intake was slightly higher in cases than non-cases (table 3), this was attenuated after adjustment for energy intake, physical activity, BMI, smoking and urban living (p=0.34). Intake of all other food groups was similar between cases and non-cases.

Table 4 shows the ORs for prostate cancer mortality in relation to baseline dietary intake. Protein intake, adjusted for age and education, and comparing the high intake (quartile 4) to the low intake (quartile 1) showed an OR of 1.32 (95% CI 0.86-2.02) and a p-trend of 0.17. The OR comparing the top quartile of 4 or more servings (equivalent to 1 or more cups) to no legume intake was 1.40 (95% CI 0.91-2.18) with a p-trend of 0.17. Additional adjustment for energy intake, physical activity, BMI, smoking and urban living attenuated the association to a p-trend of 0.93. Consuming 1-2 servings of fruit was inversely associated with prostate cancer mortality (OR 0.50, 95% CI 0.32-0.77), and this remained significant after additional adjustments for energy intake, physical activity, BMI, smoking and urban living (OR 0.52, 95% CI 0.30-0.88). Consuming more than 2 servings of fruit was not associated with prostate cancer

mortality. There were no associations between vegetable or dairy intake and prostate cancer mortality.

Discussion

Most of the epidemiologic studies on legume intake and prostate cancer have focused on soy bean intake (23) and few studies have examined the impact of non-soy legumes. Most of the legumes consumed in the U.S. are not soybeans; thus, examining the relationship of non-soy legume intake and prostate cancer is of public health significance. Additionally, few studies have examined dietary intake among populations with sufficiently large variation, such as the case in Puerto Rico, in non-soy legume intake. To put the dietary intake of our study population in perspective, we compared the intake of the men in the PRHHP with the intake of men in the Third National Health and Nutrition Examination Survey (NHANES III), a representative sample of the U.S population. Although the PRHHP dietary intake data were collected in the early 1960's whereas NHANES III was collected from 1988-1994, little information about intake of specific protein sources (i.e., animal and plant protein) is available prior to 1988 for the U.S. Daily caloric intake (2368 kcals) among the men in the PRHHP was approximately 200 kcals lower on average than for male participants in the NHANES III (2591 kcals) (24). Although total protein intake (85 grams) was also lower in this study population than in NHANES III (97 grams), the percentage of calories from protein was similar (15% NHANES III, 14% PRHHP)(25). The percentage of protein from vegetable sources was also similar (32.5% NHANES III, 30.4% in PRHHP). Despite consuming a similar percentage of protein from animal sources (67.5% NHANES III, 69.4% PRHHP), the men in the PRHHP consumed a higher percentage of dairy protein (22.9% NHANES III, 29.8% PRHHP) and a lower percentage of meat, fish, and poultry protein (44.6% NHANES III, 39.8%, PRHHP)(24).

The U.S. Department of Agriculture (USDA) recommends 3 cups of legumes per week as part of vegetable consumption for men (26). Legume intake was an average of 4.4 cups per week in the PRHHP; thus, the participants in this cohort consumed more than the recommended amount of legumes. Vegetable consumption recommended by the USDA is 3 cups per day and if legumes are counted towards this food group then vegetable consumption was 3.1 cups per day. USDA meat consumption recommendations are 6-6.5 oz per day and can include legumes. If legumes were counted towards meat consumption, then vegetable consumption was only 0.9 cups and thus legumes account for a major portion of vegetable consumption. The men in the PRHHP consumed an equivalent of 5 oz of meat excluding legumes and 7.2 oz if legumes are included. Milk consumption of 2.2 cups per day was also below the USDA recommendation of 3 cups a day.

We found no association between legume intake and prostate cancer mortality in this cohort of Puerto Rican men. This is in contrast with Jain et al who found an inverse association between prostate cancer and the combined intake of beans, lentils and nuts in a case control study in Canada (3). Similarly, a multi-center case control study showed an inverse association between legume intake and prostate cancer in African American and Chinese men, but not in white or Japanese men (27). Legumes were also inversely associated with prostate cancer in cohort of Dutch men (28). Differences may in part be due to differences in the range in legume intake; the type of legume consumed, and case selection (incident versus mortality prostate cancer cases).

We found no association between meat consumption and prostate cancer mortality and results from other epidemiologic studies have been mixed (29-33). Dairy intake was also not associated with prostate cancer mortality and although this is similar to results from some epidemiological studies, many other studies have found a positive association (34). Milk comprised much of the dairy consumption in the PRHHP men and

a potential difference with other populations might be that most of the milk consumed comes as part of the coffee consumption.

Consuming 1-2 servings of fruit was inversely associated with prostate cancer mortality; however, consuming more than 2 servings of fruit was not associated with prostate cancer mortality. Our study found no association between vegetable consumption and prostate cancer. Results from other epidemiologic studies on the relationship between fruit and vegetables and prostate cancer have been mixed (14;32;35-37). Differences in results among epidemiologic studies may in part be due to differences in specific food intakes, variation of intake, follow-up times, case selection (aggressive fatal cancer versus early stage prostate cancer), and other issues related to study design and analysis.

Cohort studies, such as the PRHHP, usually obtain their dietary information at a single point in the adult life of the participants. One assumption in prospective studies is that diet is constant. For cohort studies conducted during the 1950's, 1960's and 1970's, and among older men this may be a reasonable assumption (38). Errors, however, can be introduced if dietary habits change over time and are not recorded in the study. In our cohort of older men, we believe that variations in consumption of staple foods such as beans and peas have remained fairly constant, especially among older men. The foods examined in this study have been readily available and consumed in Puerto Rico without major changes in the market or the per capita consumption (11).

In summary, we found no association between a prospective measure of intake of protein and legumes with prostate cancer mortality in this cohort of Puerto Rican men. Consumption of legumes in the men in this cohort was approximately twice the amount of legumes consumed by men in the U.S.; thus, this population is well suited for studying the impact of legume intake. Future research should focus on legumes in relation to early stage prostate cancer, as well as the relationship of other potential dietary factors.

Note: This study was partially supported by grants from the Department of Defense (DAMD17-02-1-0252), and the National Institutes of Health (1P20CA96256-01A1, and 1R03 CA103475-01).

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Table 1. Characteristics of the Puerto Rico Heart Health Program participants according to prostate cancer mortality.

	Prostate Cancer Deaths (n=167)		Non Cases (n=9610)		Chi-square P-value
	n	%	n	%	
Age, years					0.04
35-44	3	1.8	345	3.6	
45-54	69	41.3	4839	50.4	
55-64	82	49.1	3762	39.2	
65+	13	7.8	664	6.9	
Education					0.09
No formal schooling	16	9.6	974	10.1	
Grades 1-4	51	30.5	3390	35.3	
Grades 5-8	58	34.7	2754	28.7	
Attended/completed highschool	22	13.2	1700	17.7	
More than highschool	20	12.0	786	8.2	
Living					0.52
Urban	47	28.1	2927	30.5	
Rural	120	71.9	6683	69.5	
Smoking					0.53
None	51	30.5	3236	33.7	
Past	73	43.7	4208	43.8	
Current	43	25.8	2157	22.5	
BMI (weight (kg) / height (m)^2)					0.89
Underweight (<18.5)	4	2.4	310	3.2	
Normal weight (18.5-24.9)	76	45.5	4529	47.1	
Overweight (25-29.9)	66	39.5	3609	37.6	
Obese (30+)	21	12.6	1162	12.1	
Physical activity					0.64
Quartile 1 (low)	43	25.8	2619	27.3	
Quartile 2	38	22.8	2381	24.8	
Quartile 3	46	27.5	2240	23.3	
Quartile 4 (high)	40	24.0	2370	24.7	

Table 2. Dietary intake of macronutrients of the Puerto Rico Heart Health Program participants according to prostate cancer mortality.[a]

	Prostate Cancer Deaths (n=167)	Non Cases (n=9610)	p-value
Energy (kcals)	2456 (66.7)	2379 (15.4)	0.24
Protein (g)	88.6 (2.7)	85.4 (0.6)	0.23
Animal (g)	29.2 (1.8)	29.5 (0.4)	0.86
Seafood (g)	7.4 (1.2)	7.2 (0.3)	0.88
Dairy (g)	26.7 (1.2)	24.9 (0.3)	0.12
Vegetable (g)	25.2 (.9)	23.8 (0.2)	0.12
Carbohydrate (g)	288.2 (8.4)	274.8 (1.9)	0.10
Fat (g)	97.7 (3.3)	95.4 (0.8)	0.49
Saturated (g)	36.6 (1.3)	35.6 (0.3)	0.44
Poly unsaturated (g)	14.7 (0.9)	14.6 (0.2)	0.91
Mono unsaturated (g)	38.1 (1.4)	37.2 (0.3)	0.55

[a] Adjusted for age and education

Table 3. Dietary intake of foods of the Puerto Rico Heart Health Program participants according to prostate cancer mortality.[a]

	Prostate Cancer Deaths (n=167)	Non Cases (n=9610)	p-value
Dairy[b] (servings)	4.7 (0.23)	4.4 (0.05)	0.30
Milk (4 oz)	4.3 (0.22)	4.0 (0.05)	0.19
Seafood[c] (oz)	0.6 (0.10)	0.5 (0.02)	0.59
Meats[d] (oz)	2.7 (0.22)	2.9 (0.05)	0.54
Fruits (100 g)	1.2 (0.13)	1.2 (0.03)	0.71
Vegetables[e] (1/4 c)	5.3 (0.22)	5.0 (0.05)	0.19
Legumes (1/4 c)	2.4 (0.17)	2.1 (0.04)	0.07
Coffee (1 oz)	2.8 (0.14)	2.8 (0.03)	0.91

[a] Adjusted for age and education

[b] Dairy is the sum of milk (4 oz), cheese (1 oz) and icecream (4oz)

[c] Seafood is the sum of fish, cod, and shellfish

[d] Meats is the sum of beef, pork, ham, lunch meats, sausage, pigs feet.

[e] Vegetables is the sum of legumes, starchy vegetables, other cooked and other raw vegetables

Table 4. Odds Ratios for prostate cancer mortality in relation to baseline dietary intake (167 cases among 9777 men).

	Quartiles				P-trend
	Q1	Q2	Q3	Q4	
	Macronutrients				
Calories (kcals)					
Range	≤1770	1771-2275	2276-2847	≥2848	
OR (95% CI)[a]	1.0	0.86 (0.54-1.34)	.92 (0.59-1.44)	1.28 (0.84-1.95)	0.19
OR (95% CI)[b]	1.0	0.84 (0.53-1.31)	0.89 (0.57-1.40)	1.24 (0.81-1.90)	0.23
Carbohydrates (g)					
Range	≤202	203-266	267-340	≥341	
OR (95% CI)[a]	1.0	0.98 (0.62-1.55)	1.16 (0.74-1.80)	1.38 (0.90-2.12)	0.10
OR (95% CI)[b]	1.0	0.94 (0.59-1.50)	1.09 (0.68-1.75)	1.27 (0.76-2.12)	0.29
Fat (g)					
Range	≤64	65-88	89-117	≥118	
OR (95% CI)[a]	1.0	0.84 (0.53-1.31)	0.98 (0.64-1.52)	1.07 (0.69-1.66)	0.60
OR (95% CI)[b]	1.0	0.83 (0.52-1.29)	0.99 (0.64-1.54)	1.12 (0.70-1.80)	0.49
Protein (g)					
Range	≤61	62-82	83-103	≥104	
OR (95% CI)[a]	1.0	0.96 (0.61-1.50)	1.03 (0.65-1.61)	1.32 (0.86-2.02)	0.17
OR (95% CI)[b]	1.0	0.94 (0.60-1.48)	1.02 (0.64-1.63)	1.32 (0.81-2.17)	0.22
Animal protein (g)					
Range	≤13	14-23	24-40	≥41	
OR (95% CI)[a]	1.0	0.75 (0.49-1.16)	0.84 (0.55-1.29)	0.86 (0.56-1.33)	0.61
OR (95% CI)[b]	1.0	0.78 (0.49-1.24)	0.91 (0.55-1.51)	1.01 (0.52-1.96)	0.94
Vegetable protein (g)					
Range	≤16	17-23	24-31	≥32	
OR (95% CI)[a]	1.0	1.31 (0.86-2.00)	1.15 (0.74-1.81)	1.34 (0.86-2.09)	0.28
OR (95% CI)[b]	1.0	1.27 (0.82-1.96)	1.07 (0.66-1.75)	1.19 (0.66-2.13)	0.70
Dairy protein (g)					
Range	≤13	14-22	23-34	≥35	
OR (95% CI)[a]	1.0	1.19 (0.76-1.88)	1.27 (0.82-1.95)	1.35 (0.87-2.10)	0.18
OR (95% CI)[b]	1.0	1.15 (0.71-1.88)	1.21 (0.70-2.10)	1.25 (0.57-2.73)	0.59
Seafood protein (g)					
Range	0	≥1			
OR (95% CI)[a]	1.0	0.94 (0.67-1.33)			0.73
OR (95% CI)[b]	1.0	0.85 (0.49-1.48)			0.56
	Foods				
Dairy (servings)					
Range	≤2	3-4	5-6	≥7	
OR (95% CI)[a]	1.0	1.27 (0.84-1.91)	0.97 (0.61-1.55)	1.41 (0.91-2.17)	0.23
OR (95% CI)[b]	1.0	1.33 (0.84-2.11)	1.10 (0.59-2.04)	1.75 (0.76-4.05)	0.27
Meat (oz)					
Range	0	1-2	3-4	≥5	
OR (95% CI)[a]	1.0	0.74 (0.48-1.12)	0.90 (0.59-1.36)	0.85 (0.55-1.32)	0.53
OR (95% CI)[b]	1.0	0.81 (0.52-1.26)	1.10 (0.66-1.83)	1.27 (0.62-2.63)	0.60
Seafood (oz)					
Range	0	≥1			
OR (95% CI)[a]	1.0	0.96 (0.67-1.39)			0.84

OR (95% CI) [b]	1.0	0.79 (0.44-1.41)			0.43
Fruit (100 g)					
Range	0	1-2	≥3		
OR (95% CI) [a]	1.0	0.50 (0.32-0.77)	0.98 (0.65-1.46)		0.34
OR (95% CI) [b]	1.0	0.52 (0.30-0.88)	1.13 (0.45-2.79)		0.30
Vegetables (1/4 c)					
Range	≤3	4-5	6-8	≥9	
OR (95% CI) [a]	1.0	1.48 (0.97-2.26)	1.27 (0.83-1.93)	1.37 (0.88-2.13)	0.24
OR (95% CI) [b]	1.0	1.56 (0.94-2.59)	1.41 (0.71-2.83)	1.61 (0.68-3.83)	0.48
Legumes (1/4 c)					
Range	0	1-2	3	≥4	
OR (95% CI) [a]	1.0	1.25 (0.84-1.88)	1.05 (0.63-1.77)	1.40 (0.91-2.18)	0.17
OR (95% CI) [b]	1.0	1.14 (0.72-1.79)	0.90 (0.48-1.69)	1.06 (0.48-2.32)	0.93

[a] adjusted for age(35-44, 45-54, 55-64, 65+ years), education (no formal schooling, grades 1-4, grades 5-8, attended/completed highschool, more than highschool).

[b] adjusted for age, education, body mass index (underweight, normal weight, overweight, obese), living (urban, rural), physical activity (quartiles), smoking (never smoker, current smoker, past smoker) and residual energy intake. Calories not adjusted for energy intake.

ELSEVIER

Skin Color and Mortality Risk Among Men: The Puerto Rico Heart Health Program

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PURPOSE: To examine the association between skin color and all-cause and cardiovascular disease (CVD)-related mortality risk before and after adjusting for selected characteristics and risk factors, we used data on 5,304 men with information on skin color at Exam 3 of the Puerto Rico Heart Health program (PRHHP), a longitudinal study of the incidence of coronary heart disease in Puerto Rican men.
METHODS: Mortality was ascertained using hospital and physician records, postmortem records, death certificates, and information from the next of kin.
RESULTS: Dark-skinned men exhibited higher age-adjusted mortality rates than light skinned men (10.1 vs. 8.8/10,000 population). There was no association between skin color and all-cause and CVD-related mortality. However, the association between skin color and all-cause mortality varied with area of residence (p for interaction = 0.05). Among men living in urban areas, the risk of all-cause mortality was 28% (95% confidence interval, 1.02–1.61) greater among dark-skinned men than their light-skinned counterparts after adjusting for age, education, BMI, physical activity, and the presence of diabetes. There was no association between skin color and CVD mortality in urban men. Neither all-cause nor CVD mortality was associated with skin color among rural men.
CONCLUSION: Our results suggest that skin color may be capturing environmental dynamics that may influence mortality risk among Puerto Rican men.
Ann Epidemiol ■;■:■. © 2007 Elsevier Inc. All rights reserved.

KEY WORDS: Skin Color, Mortality, Puerto Rico, Area Of Residence, Hispanics.

INTRODUCTION

In the United States, Hispanics (629.3 per 100,000) have lower age-adjusted all-cause death rates than non-Hispanics (856.5; 1). However, when Hispanic data are disaggregated, a different pattern emerges: Puerto Ricans (766.2) exhibit higher age-adjusted all-cause death rates than Mexican Americans (612.8) and Cubans (524.1) but similar to Hispanics from other countries (761.8). Moreover, a similar pattern has been observed for other health outcomes such as self-rated health and activity limitation status, with Puerto Ricans exhibiting the worst outcomes (2). These results suggest that heterogeneity among Hispanic subgroups often is lost as the result of data aggregation (3). This aggregation also masks the existing racial heterogeneity among Hispanics (4).

Although few studies have examined the effect of skin color on health among Hispanics (5–7), these studies suggest that health differences exist according to skin color. For example, studies on skin color measured using skin color tiles show that dark-skinned Puerto Rican men had a greater prevalence of left ventricular hypertrophy and slightly higher systolic blood pressure than their light-skinned counterparts (5, 6). These studies underscored the role of genetic and environmental determinants of differences between light- and dark-skinned men while recognizing the limitations of the data. Furthermore, Landale and Oropesa (7) found that mothers' skin color was associated with low birth weight in Puerto Rican infants in selected states in the Northeast region of the United States but not in Puerto Rico or New York City. These findings parallel existing evidence among African Americans, with dark-skinned African-American subjects exhibiting worse health outcomes than light-skinned African Americans (8–11). Specifically, these studies found a positive association between darker skin color and hypertension. Thus, it is possible that skin color affects the opportunities and resources (or lack thereof) for Hispanics, and this in turn may influence their health status as it does for African Americans. Therefore, the investigation of skin color, as a proxy for racial categorization, among Puerto Ricans could provide insight into

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Received ■; accepted ■.

360 Park Avenue South, New York, NY 10010
1047-2797/07/$–see front matter
doi:10.1016/j.annepidem.2006.11.002

Selected Abbreviations and Acronyms

PRHHP = Puerto Rico Heart Health program
CVD = cardiovascular disease
CHD = coronary heart disease
BMI = body mass index
RR = relative risk
CI = confidence intervals

how race works to create health disparities in this population. This racial categorization may be associated with socially patterned experiences such as racism and discrimination.

Data from the Puerto Rico Heart Health Program (PRHHP) study affords the opportunity to investigate the association between skin color and mortality, all-cause and cardiovascular disease (CVD) related deaths in Puerto Rican men before and after adjusting for selected covariates. Specifically, we use data on skin color obtained during Exam 3 and on mortality obtained at the 12-year follow up of the PRHHP study to investigate: (i) whether skin color measured at Exam 3 is associated with all-cause and CVD-related mortality and (ii) whether these relationships differ by area of residence. We hypothesize that all-cause and CVD-related mortality may be greater among dark-skinned men as compared with light-skinned men. In addition, because of the difference in social structure between rural and urban areas, we expect that this association could vary with area of residence. Specifically, those living in urban areas at baseline may exhibit stronger associations between mortality and skin color than for those living in rural areas.

METHODS

The PRHHP was designed to examine the epidemiology of coronary heart disease (CHD), including morbidity and mortality associated with CHD in urban and rural Puerto Rican men 35 to 79 years of age at baseline (12, 13). The study recruited men in March 1965 and followed them up to August 1981. Men were recruited from three urban and four rural municipalities in the northeast part of Puerto Rico using enumeration districts obtained from the U.S. Census (13). The study's response rate was 80% of the enumerated individuals at baseline constituting a sample of 9824 men, including 6843 from urban municipalities and 2981 from rural areas. This analysis was limited to participants at Exam 3 (1971–1975) without CHD for whom information on skin color was obtained during the examination. This criteria yielded a sample size of 5304 men between the ages of 40 to 84 years at Exam 3, with the majority residing in urban areas ($n = 3671$).

All men completed an extensive interview and a comprehensive physical examination, electrocardiogram, and laboratory exams at baseline. Information on demographic characteristics, medical history, and health-related behaviors was collected through a personal interview.

Skin color was assessed by matching the skin color of the upper inner arm to a set of photographic color tiles, the von Luschan color tiles (5, 6). These color tiles were used by anthropologists at the time of the study and consisted of 30 colored tiles representing shades of skin color from very light to very dark. The color tiles were matched to each participant's skin color. Recent research found a correlation of 0.95 between measures using electron energy loss (or reflectance spectrophotometry) and the von Luschan's scale adding validity to the use of the latter scale (14). To minimize measurement error, all skin color measurements were made by the same examiner. The selection of the upper inner arm avoided any error that may be caused by exposure of the skin to the tropical sun in Puerto Rico. According to previous studies (5, 6), the data on skin color were dichotomized with values 23 to 30 in the scale classified as dark skin and light skin otherwise.

Mortality was ascertained in study participants for whom complete information on skin color was available at the time of the third examination and followed for 6.25 years after that examination. Cause of death was determined using hospital and physician records, postmortem records, death certificates and information from the next of kin. Vital status at year 12 was completed on all but 9 subjects from the initial examination. At the completion of the study (August 1981), there were 552 deaths in participants who had data on skin color and did not have CHD at Exam 3, with 471 deaths occurring in light-skinned men and 81 deaths in dark-skinned men. For these analyses, deaths were classified according to underlying cause of death as all-cause and related to CVD (cerebrovascular accident, cerebrovascular disease, coronary heart disease and sudden death).

Consistent with previous studies using these data (15, 16), age, marital status, education, area of residence, smoking, body mass index (BMI), physical activity, alcohol consumption, cholesterol levels, hypertension and diabetes status were included as covariates. Marital status (single, married, widowed, and divorced or separated), education (less than 8th grade; attended or completed high school; attended or completed college), area of residence (urban/rural), smoking (current, former and never), and alcohol consumption obtained from a 24-hour diet recall interview (none; 1–39 g; and more than 40 g) were collected at baseline, whereas age (continuous), BMI (≤18.5; 18.5–24.9; 25–29.9; and ≥30), physical activity (physical activity index tertiles), cholesterol (≤200 mg/dL; 200-239 mg/dL; and ≥240 mg/dL), hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or currently taking antihypertensive medications) and diabetes (having a nonfasting glucose level ≥140 mg/dL or currently taking

medications for diabetes) were collected at baseline and verified at Exam 3. There was little difference in these measures between Exams 1 and 3. For example, BMI at Exam 1 was 25.1 kg/m (SE = 0.05) and at Exam 3 was 25.5 kg/m (SE = 0.05). This was also true for diastolic (82.2 [SE = 0.16] and 83.8 [SE = 0.16] mmHg at Exams 1 and 3, respectively) and systolic blood pressure (132.0 [SE = 0.30] and 133.6 [SE = 0.32] mm Hg at Exams 1 and 3, respectively).

Statistical Analysis

Descriptive statistics for selected characteristics of the population were calculated by skin color, and further by all-cause and CVD-related mortality. To determine statistical significance of differences, chi-square tests were used. Poisson regression was used to estimate age-adjusted mortality rates per 10,000 population by skin color and further by area of residence. PROC GENMOD (17) was used to calculate relative risk (RR) and their 95% confidence intervals (95% CI) for all-cause and CVD-related mortality risk in men with dark skin relative to those with light skin, before and after controlling for selected characteristics. In the analysis for CVD, deaths for other causes were treated as censored. The interaction between skin color and area of residence was tested by including the appropriate interaction terms in the models for all-cause and CVD-related mortality. These analyses were repeated for skin color by area of residence (urban and rural). Two-sided p values of <0.05 were considered statistically significant. Analyses were performed using SAS V9.1.3 (18).

RESULTS

In general, light-skinned Puerto Rican men were more educated, more likely to live in rural areas, have higher cholesterol levels, and a lower prevalence of hypertension than their dark skinned peers (all p-values <0.05; Table 1). There was no association of marital status and alcohol consumption with skin color (data not shown).

Table 2 shows selected characteristics for those who died and those who did not die according to skin color among Puerto Rican men. There were a total of 552 deaths, with 471 among light-skinned men and 81 among dark-skinned men. When compared with survivors, those who died were more likely to be older, underweight, and have hypertension and diabetes regardless of skin color. In addition, light-skinned men who died were more likely to be less educated, whereas dark-skinned men were more likely to live in urban areas and never smoke. With regard to CVD, light- and dark-skinned men who died were older and were more likely to have hypertension and diabetes than those who did not die. Light-skinned men who died from CVD had greater levels of income, were more likely to be underweight, and had higher cholesterol levels, whereas dark-skinned men were more likely to be never smokers as compared with those who did not die.

TABLE 1. Selected characteristics at baseline in participants of the PRHHP by skin color among Puerto Rican Men

Characteristics	Skin color		
	Light ($n = 4633$)	Dark ($n = 671$)	p Value[a]
Age, years			
40–54	24.8	21.5	
55–64	51.2	53.5	
65–79	24.0	25.0	0.17
Education			
< 8 years	73.1	82.4	
Attended or completed high school	17.7	14.8	
Attended or completed college	9.2	2.8	<0.0001
Annual income			
⩽3000	49.2	47.8	
>3001	50.8	52.2	0.48
Area of residence			
Urban	66.8	85.5	
Rural	33.2	14.5	<0.0001
Smoking			
Current	43.5	43.1	
Former	22.8	21.0	
Never	33.7	35.9	0.42
BMI			
<18.5	2.9	3.2	
18.5–24.9	42.5	41.8	
25.0–29.9	41.0	39.6	
⩾30	13.6	15.4	0.59
Cholesterol			
<200 mg/dL	56.0	62.5	
200–239 mg/dL	32.1	29.4	
⩾240 mg/dL	11.9	8.1	0.001
Physical activity (tertile)			
Low	37.4	33.5	
Middle	30.7	30.5	
High	31.9	36.0	0.06
Hypertension (yes)	20.1	24.9	0.004
Diabetes (yes)	18.8	17.9	0.59

[a]p values for Chi-square comparing light- versus dark-skinned men.

Dark-skinned men exhibited higher age-adjusted mortality rates (10.1 per 10,000 population) than light-skinned men (8.8 per 10,000 population, $p = 0.23$; Fig. 1). This pattern persists for men residing in urban areas (7.5 for dark skin per 10,000 population versus 6.2 for light skin, $p = 0.09$). However, the opposite was true for men living in rural areas: Light skinned men had at least twice the risk of dying compared with their dark skinned counterparts (14.3 vs. 7.0 per 10,000 population, $p = 0.10$).

Table 3 shows the relative risk and their 95% CI for the association between skin color and mortality, all-cause and CVD-related mortality, before and after adjusting for selected covariates. There was no association between skin color and all-cause and CVD-related mortality risk among

TABLE 2. Selected characteristics at baseline in participants in Exam 3 according by skin color among Puerto Rican Men: The PRHHP

Characteristics	Light (n = 4,633)			Dark (n = 671)		
	Did not die (n = 4,62)	All-cause (n = 471)	CVD (n = 209)	Did not die (n = 590)	All-cause (n = 81)	CVD (n = 37)
Age, years						
40–54	26.1	13.8	12.4	22.5	13.6	8.1
55–64	52.4	40.1	35.9	55.1	42.0	45.9
65–79	21.6	46.1[†]	51.7[†]	22.4	44.4[†]	46.0[a]
Education						
<8 years	72.4	79.2	79.9	81.7	87.6	91.9
Attended or completed high school	18.2	14.0	13.4	15.3	11.1	8.1
Attended or completed college	9.4	6.8[a]	6.7	3.1	1.2	0
Annual income						
⩽3,000	49.9	42.9	42.9	48.1	45.4	35.3
>3,001	50.1	57.1[b]	57.1[a]	51.9	54.6	64.7
Area of residence						
Urban	67.0	65.8	67.5	84.4	93.8	94.6 [EQ1]
Rural	33.0	34.2	32.5	15.6	6.2[a]	5.4
Smoking						
Current	43.3	46.1	41.2	44.1	35.8	27.0
Former	22.8	22.7	26.3	21.7	16.0	18.9
Never	33.9	31.2	32.5	34.2	48.2[a]	54.1[a]
BMI						
<18.5	2.5	6.5	3.9	2.1	11.1	5.4
18.5–24.9	42.4	43.0	32.7	40.9	48.2	43.2
25.0–29.9	41.5	36.4	43.9	41.4	25.9	35.1
⩾30	13.6	14.1[a]	19.5[a]	15.5	14.8[a]	16.2
Cholesterol						
<200 mg/dL	55.9	56.7	53.8	61.9	67.5	58.3
200–239 mg/dL	32.4	29.2	28.6	30.1	23.7	30.6
⩾240 mg/dL	11.7	14.1	17.6*	8.0	8.8	11.1
Physical activity (tertile)						
Low	36.5	45.8	52.2	32.5	40.7	51.3
Middle	31.2	26.4	25.1	30.9	27.2	21.6
High	32.4	27.7[†]	22.7[†]	36.6	32.1	27.0
Hypertension						
Yes	18.6	33.3	44.0	22.7	40.7	64.9
No	81.4	66.7[†]	56.0[†]	77.3	59.3[a]	35.1[†]
Diabetes						
Yes	17.7	28.5	37.3	16.3	29.6	32.4
No	82.3	71.5[†]	62.7[†]	83.7	70.4[a]	67.6[a]

p values comparing those who died from all cause and from CVD to those who did not die [a]<0.05 [b]<0.001.

Puerto Rican men. However, the association between skin color and all-cause mortality varied with area of residence (p for interaction = 0.05). Among men living in urban areas, the risk of all-cause mortality was 32% greater among men with dark skin compared with their light-skinned counterparts. This association remains nearly unchanged (RR = 1.28; 95%CI = 1.02–1.61) after adjusting for age, education, BMI, physical activity, diabetes, and area of residence. There was no association between skin color and CVD-related mortality in Puerto Rican men living in urban areas. Similarly, neither all-cause nor CVD-related mortality was associated with skin color among men living in rural areas.

Because of the observed urban–rural difference in mortality among light skinned men (6.2 per 10,000 in urban vs. 14.3 in rural), we repeated the analyses for light-skinned and dark-skinned men separately to evaluate the effect of area of residence on all-cause mortality risk (data not shown in the tables). After adjustment for age, education, BMI, physical activity, hypertension, and diabetes, there was no association between area of residence and all-cause mortality among light-skinned men. However, although the number of events was small for dark-skinned men in both urban and rural areas, dark-skinned men living in urban areas had a mortality risk 3.11 times (95% CI, 1.31–7.39) greater than dark-skinned men living in rural areas. This finding confirms

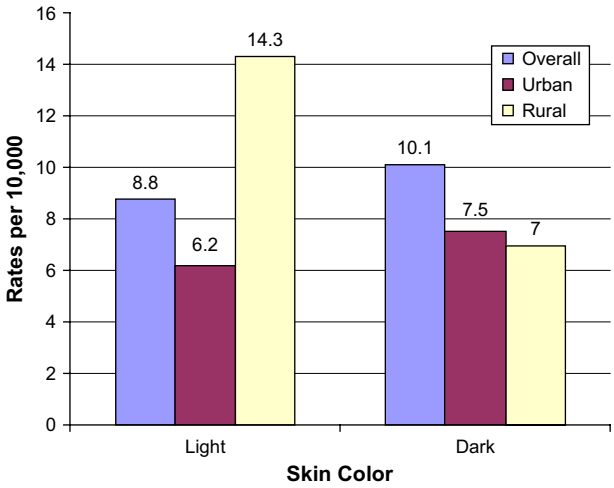

FIGURE 1. Age-adjusted death rates according to skin color and area of residence: The PRHHP Study.

our skin color/area of residence interaction and suggests that skin color dynamics between the urban and rural areas must be different with urban settings possibly affording a higher risk for dark-skinned men.

DISCUSSION

Our results show no association between skin color and all-cause or CVD-related mortality among Puerto Rican men. However, the association between skin color and all-cause mortality varies with area of residence: Dark-skinned Puerto Rican men living in urban areas at baseline have a higher risk of dying from all-cause mortality than their light skinned counterparts. This association was not observed between skin color and CVD-related mortality in men living in urban areas. There was no association between skin color and all-cause or CVD-related mortality for Puerto Rican men living in rural areas.

Results from studies examining the relationship between skin color and health outcomes among African Americans have been inconsistent (8, 19–21). For example, early studies found an association between skin color and hypertension, with dark skin being associated with hypertension (8). The study proposed a biological mechanism based on the presence of tyrosine and dopamine in both melanin and norpeinephrine–epinephrine (8). Later studies found no association between skin color and blood pressure among African Americans. These studies suggest the possibility of confounding between skin color and socioeconomic status (SES; 19–21). Specifically, dark-skinned African Americans tend to be more likely to be less educated and to have a lower income than their light-skinned counterparts. This study also shows that dark-skinned Puerto Rican men were less educated than their lighter-skinned counterparts. Previous studies using the PRHHP data also have found an association between skin color and the prevalence of left ventricular hypertrophy and systolic blood pressure, with darker-skinned Puerto Rican men exhibiting worse outcomes than their light skinned counterparts (5, 6).

The few studies that focused on the association between skin color and mortality have yielded mixed results (22, 23). For example, Keil et al. (22), using data from the Charleston Heart Study (CHS) in South Carolina, found an association between skin color and all-cause mortality among black men and women with light-skinned men and women exhibiting a small increase in risk of dying when compared with their dark-skinned counterparts.

TABLE 3. Relative risk (all-cause and CVD) and their 95% confidence intervals (CI) for Puerto Rican men by skin color and area of residence

		Relative risk (95% CI)			
		All-Cause		CVD	
Characteristics	Total no. of deaths	Unadjusted	Adjusted[a]	Unadjusted	Adjusted
Skin[b]					
Dark	81	1.19 (0.95–1.48)	1.18 (0.95–1.47)	1.23 (0.88–1.73)	1.21 (0.85–1.72)
Light	471	1.00	1.00	1.00	1.00
Urban					
Skin					
Dark	76	1.32 (1.05–1.67)	1.28 (1.02–1.61)	1.36 (0.95–1.95)	1.33 (0.94–1.90)
Light	310	1.00	1.00	1.00	1.00
Rural					
Skin					
Dark	5	0.49 (0.21–1.17)	0.52 (0.22–1.24)	0.45 (0.11–1.81)	0.52 (0.13–2.13)
Light	161	1.00	1.00	1.00	1.00

[a]Adjusted: Overall: Age, BMI, physical activity, hypertension, diabetes and area of residence; urban: age, education (all-cause), BMI, physical activity and diabetes; Rural: Age, BMI, physical activity (CVD), hypertension and diabetes.
[b]*p*-Interaction between skin color and rural/urban in the adjusted models: all-cause: 0.05; CVD: 0.23.

Using the same CHS data, Knapp et al. (23) examined the association of skin color and cancer mortality. The authors restricted the sample to men only and included a high SES black men supplemental sample. The study found that light skin was protective against cancer mortality only among the high SES subsample. This finding suggested that skin color may be a multidimensional marker that may capture biological and social phenomenon to affect health and disease processes.

Our study did not find an association between skin color and all-cause or CVD-related mortality among Puerto Rican men. However, the association between skin color and all-cause mortality varied with area of residence: Dark-skinned Puerto Rican men living in urban areas had a higher risk of dying of all-cause mortality compared with their light-skinned counterparts. Although there was no association for men living in rural areas, dark skin appears to be protective in men living in rural areas. Moreover, dark-skinned men living in urban areas had a higher all-cause mortality risk than their counterparts living in rural areas. These findings did not support skin color as a genetic marker among Puerto Rican men and the interaction between skin color and area of residence could reflect the social dynamic of skin color among Puerto Ricans. Although Puerto Rico, at the time of the study, retained many of its traditional values, culture, and lifestyle, the difference between urban and rural areas in terms of social and economic structure was evident. For example, the urban areas exhibited an industrial growth, a more distinct difference in wealth and poverty, and a less-cohesive social structure than the rural areas (12). Consistent with these changes, it is possible that differential treatment by skin color may have taken place in Puerto Rico as it was happening in the United States. Specifically, evidence suggests that skin color among Puerto Rican (dark or nonwhite vs. light or white classification) in New York City (4, 24–26) may have been influencing their life chances in terms of education, income, and occupation since the mid 1970s. Similarly, evidence suggests that skin color has been considered a marker of discrimination among African Americans with darker skinned individuals reporting higher levels of discrimination than their lighter skinned peers (27, 28). Therefore, it is possible that skin color may have acted as a marker for discrimination among Puerto Ricans.

We did not find an association between skin color and CVD-related mortality in Puerto Rican men. However, although previous studies have not examined the association between skin color and CVD-related mortality, previous studies have examined the incidence and mortality of CHD (12, 19). Specifically, Gordon et al. (29) found a lower incidence of CHD in Puerto Rican men as compared to U.S. whites in the Framingham study and Hawaiians in the Honolulu study. Moreover, Garcia-Palmieri et al (12), when using the PRHHP data, did not find an urban-rural difference in CHD mortality during a 12-year period. Although our null findings may be the result of the small number of deaths related to CVD, they are consistent with prior work (12, 29).

Among the strengths of our study are the longitudinal design; population-based nature and homogeneity of the sample in terms of characteristics and geographic location; and the availability of information on underlying causes of death, prevalent disease at baseline, and cardiovascular risk factors. Important limitations are the small sample size for the rural area and the small number of events. However, our null findings are consistent with a previous study using these data to examine association between area of residence and mortality (12). In addition, there was very little movement from rural to urban areas and vice versa. For example, between Exams 1 and 2 only 1.3% of the PRHHP men changed their area of residence. This proportion was 1.7% between Exams 1 and 4. Therefore, it is unlikely that our findings are solely the result of the small sample size and number of events. Nonetheless, lack of power may have hindered our ability to detect an association, specifically for CVD-related mortality. Another limitation was the exclusion of 4,520 men as the result of a loss to follow up (n = 1506) at Exam 3, presence of CHD at Exam 3 (n = 421) or lack of data on skin color (n = 2410). This exclusion could have biased our results. We compared the distribution of risk factors between participants with and without skin color information and the only significant differences were for BMI and physical activity. Men without skin color data were more likely to be underweight and less physically active. However, there was no difference in all-cause mortality risk between men with and without skin color information. Therefore, it is very unlikely that their exclusion could have affected the results. Although the measurements of skin color were taken 6 years before the mortality assessments, skin color is likely to remain relatively stable over time (30–34). However, if skin color changed substantially during this time, and thus, led to more or less discrimination, our results regarding associations of skin color with mortality could have been either underestimated or overestimated. Moreover, it is possible that the examiner was not blinded to the social status of the participants and was more likely to record high social status participants as light skinned. However, this is unlikely, because social status in the PRHHP was based on self-reported education, occupation, and income at baseline and not on data originated from the examiner at Exam 3. Moreover, if this bias occurred, it would have underestimated our results. Similarly, it is possible that social status was associated with sun exposure with high social status men being less likely to be exposed to sun, and thus, be more likely to appear lighter than they would if exposed to the sun. Again, this may have underestimated our results.

Our study found that skin color was associated with an increase risk of all-cause mortality among urban Puerto Rican

men only. Dark-skinned men exhibited a higher risk of dying than their light-skinned counterparts. Our results suggest that skin color may have captured environmental dynamics that may have influenced mortality risk in this homogenous population. Given the U.S. influence in Puerto Rico during the past 30 years (i.e., racial dynamics), research replicating these results in Puerto Rico is imperative.

UNCITED REFERENCES

The following reference is uncited: 1

The Puerto Rico Heart Health Program (PRHHP) was conducted and supported by the NHLBI in collaboration with the PRHHP Registry Investigators. In addition, this work was supported by the National Institute Dental and Craniofacial Research Grant K22DE15317 (LNB), the Robert Wood Johnson Health and Society Scholars Program (LNB), the Department of Defense DAMD17-02-1-0252 (CJC), and the National Institutes of Health 1P20CA96256-01A1 (CJC) and 1R03 CA103475-01 (CJC). The authors would like to thank Dr. Paul Sorlie for his helpful comments on an early draft of the manuscript and Mr. Sean Coady for his help getting the data. The manuscript was prepared using a limited access dataset obtained by the NHLBI and does not necessarily reflect the opinions or views of the PRHHP Registry or the NHLBI.

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Association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms in older American men: findings from the third National Health And Nutrition Examination Survey

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Accepted for publication 2 February 2005

OBJECTIVES

To examine the association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms (LUTS) in older men.

SUBJECTS AND METHODS

The study included 2797 men participating in the Third National Health and Nutrition Examination Survey (NHANES III), who were aged ≥60 years. During an interview, LUTS, smoking history, alcohol consumption and physical activity were assessed. Cases comprised men with at least three of the symptoms of nocturia, hesitancy, weak stream and incomplete emptying. Men who had had prostate surgery unrelated to cancer were not included as cases. Controls were men with no symptoms or surgery. We adjusted for age and race in logistic regression models and used sampling weights to account for selection probability.

RESULTS

Current cigarette smokers had no higher odds of LUTS than 'never' smokers, but former heavy smokers (≥ 50 pack-years) had a higher odds of LUTS than never smokers (odds ratio 2.01; 95% confidence interval 1.04–3.89). Men who drank alcohol daily had a lower chance of LUTS than non-drinkers (0.59; 0.37–0.95; *P* trend, 0.07). All levels of moderate and vigorous activity were statistically significantly inversely associated with LUTS (*P* trend, 0.06), whereas men who reported no leisure-time physical activity had a greater odds of LUTS (2.06; 1.26–3.39).

CONCLUSIONS

Moderate alcohol consumption and physical activity may be protective against LUTS. Current cigarette smoking was not consistently associated with the condition. The possible association in former smokers warrants further investigation.

KEYWORDS

NHANES III, LUTS, smoking, physical activity, alcohol consumption

INTRODUCTION

LUTS are a common bothersome condition in older men. Although BPH is thought to be one cause of these symptoms not all men with symptoms have an enlarged prostate [1]; changes in the tone of prostate and bladder smooth muscle may also contribute to these symptoms. Despite the high prevalence of LUTS not much is known about their causes. Age is the only well-established risk factor, but it has been hypothesized that common lifestyle factors such as smoking, consumption of alcohol, or physical inactivity might contribute to the symptoms.

While physical activity generally has been found to be inversely associated with the prevalence of LUTS [2,3] the associations of cigarette smoking and alcohol consumption with LUTS are more controversial. Most studies found either no [3–8] or a positive [9–11] association between cigarette smoking and LUTS. Fewer studies have evaluated the association of alcohol intake with LUTS; two studies reported an inverse association [4,11] whereas in others there were positive associations [3,7,9].

The Third National Health and Nutrition Examination Survey (NHANES III) is a large American cross-sectional study conducted between 1988 and 1994. Using the data collected in NHANES III, we evaluated the association of cigarette smoking, alcohol consumption and physical activity with LUTS in a multi-ethnic group of older men representative of the USA.

SUBJECTS AND METHODS

NHANES III is a nationally representative cross-sectional study of the non-institutionalized civilian USA population conducted between 1988 and 1994 [12]. A multistage probability sampling design was used with oversampling of non-Hispanic blacks, Mexican-Americans and older participants. Subjects participated in an interview conducted at home and had an extensive physical examination. In the present analysis we included 3117 men who were aged ≥60 years at participation. Of these, we excluded those men with a mobility impairment (103) or who were not self-respondents (133); we further excluded 84 men who reported during the interview of having had a diagnosis of prostate cancer at

some point before the interview. The remaining 2797 men were included in the analysis.

During the interview, all men who were aged ≥60 years were asked to report the following symptoms, which are part of the AUA Symptom Index [13]: (a) How many times per night do you usually get up to urinate (pass water)? ('nocturia'); (b) when you urinate (pass water), do you usually feel like you have not completely emptied your bladder? ('incomplete emptying'); (c) do you usually have trouble starting to urinate (pass water)? ('hesitancy'); and (d) has the force of your urinary stream of water decreased over the years? ('weak stream'). In the present analysis, men were considered as having LUTS if they reported at least three of the four symptoms. Nocturia was included as a symptom when men had to get up at least twice per night. Men were also asked if they had ever had surgery for their prostate not related to cancer. Those men who reported such surgery were excluded from the cases because removing the hyperplastic tissue may have reduced or eliminated symptoms. The controls were men who reported none of the four symptoms and had never had prostate surgery unrelated to cancer. Men with only one or two symptoms were excluded from the analysis to increase the specificity of the LUTS definition. In a cohort of similarly aged men unselected for urological problems and in which the AUA Symptom Index was administered [11], the Pearson correlation coefficient between the AUA symptom score and the index using only the four symptoms of the abbreviated score was 0.7 ($P < 0.001$). The agreement between using as the threshold a score of 3 or 4 on the abbreviated index and using a score of 15+ on the full index as the indicator of high moderate/severe LUTS was 69%.

Smoking history was assessed during the interview and men were classified according to their smoking habit into current (1–34, or ≥35 cigarettes/day), former, or never smokers. We also calculated pack-years of smoking from smoking history, a pack-year being defined as 20 cigarettes/day for 1 year. The consumption frequency of alcoholic beverages (beer, wine, liquor) during the past month was assessed using a food-frequency questionnaire during the interview. This method captures long-term habits of alcohol consumption. We categorized men into those who consumed none of these three alcoholic beverages, those who drank up to once per week, more than once per week but less than once per day, and those who drank alcohol once a day or more. During the physical examination at the Mobile Examination Center a 24-h dietary recall was administered, which assessed the amount of alcohol consumed during the previous day. From these data, the daily intake of alcohol (in grams) was calculated. We grouped men as having an intake of 0, 1–15, 16–37 or ≥38 g/day. Furthermore the type and frequency of leisure-time physical activity in the past month were ascertained during the interview. Physical activities were coded and classified by rate of energy expenditure (i.e. by intensity) according to a standardized coding scheme developed by Ainsworth *et al.* [14]. Men were grouped by their weekly frequency of moderate and vigorous activity, defined as walking, jogging or running, biking, swimming, aerobics, dancing, calisthenics, gardening, lifting weights, and other physical activities, if the metabolic equivalent of the activity compared to at rest (METs) was >2.4 for men aged 60–64, >1.9 for men aged 65–79, or >1.25 for men aged > 79 years. We further evaluated the frequency of vigorous activity only, which was defined as walking (for men aged > 79), jogging or running (all men), biking (for men aged > 64), swimming (all men), aerobics (all men), dancing (for men aged > 64), calisthenics (for men aged > 64), gardening (for men aged > 64), lifting weights (for men aged > 79), and other physical activity if METs were >5.9 for men aged 60–64, >4.7 for men aged 65–79, or >2.9 for men aged > 79 [15]. The waist circumference of the participants was measured during the physical examination. Men were considered to have a history of hypertension if they currently used medication to treat hypertension or if they were told by their doctor on two occasions that they had hypertension/high blood pressure.

The results were analysed statistically using SAS v8.1 (SAS Institute, Cary, NC) and SUDAAN [16] software. We used sample weights that took into account several features of the NHANES III survey, i.e. the specific probabilities of selection for the individual domains that were over-sampled as well as non-response and differences between the sample and the total USA population [12]. Logistic regression was used to calculate the odds ratio (OR) and 95% CI of LUTS for cigarette smoking, alcohol consumption and physical activity. In the logistic regression models, we adjusted for age (5-year categories) and race (non-Hispanic black, non-Hispanic white, Mexican-American, other). We further included in the models the waist circumference (continuous variable) as a possible confounder, and mutually adjusted cigarette smoking, alcohol consumption and physical activity. Trends for alcohol consumption and physical activity were tested by assigning to each man the median value for the exposure category into which he fell and modelling this term as a continuous variable, the coefficient for which was evaluated by the Wald test.

RESULTS

Of the 2797 men in the analysis, 28.8% had no LUTS and had never had prostate surgery (controls), 46.7% reported one or two symptoms and 10.3% reported three or four symptoms (cases). Men with LUTS were older than men in the control group and had fewer years of education (Table 1). These men also drank less alcohol, but smoking patterns and weekly frequency of physical activity did not differ.

Men who currently smoked up to 35 cigarettes/day had no greater odds of LUTS, but there was insignificantly greater odds of LUTS in men who smoked ≥35 cigarettes/per day (Table 2). However, this association was strongly attenuated after adjusting for waist circumference, the frequency of alcohol consumption, and the frequency of moderate and vigorous activity. Of these factors, waist circumference caused the strongest attenuation of the OR for heavy smoking. Former smokers had a slightly but not statistically significant greater odds of LUTS than never smokers. Men who had ever smoked ≥50 pack-years had a higher odds of LUTS than never smokers. This association was limited to former smokers; there was no association among current smokers who had smoked ≥50 pack-years. Further adjustment for waist circumference, but not for hypertension, attenuated the association of pack-years with LUTS in both ever and former smokers.

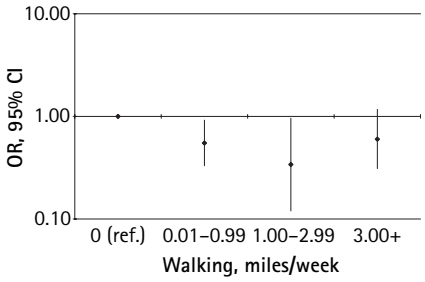
There was an inverse association between the frequency of alcohol consumption and LUTS in this group of older men (Table 2). Compared to non-drinkers, men who drank alcohol daily had a significantly lower odds of LUTS. This association was not substantially altered after

TABLE 1 Age-adjusted baseline characteristics of men aged ≥60 years in the NHANES III, 1988–94

Factor	Controls	Cases	P
Unweighted sample size	715	320	
% of total sample	28.8	10.3	
Mean (SEM)			
Age, years	67.6 (0.3)	71.0 (0.6)	<0.001*
Current waist size, cm	100.4 (0.66)	101.2 (0.65)	0.46*
Years of education	11.3 (0.2)	10.4 (0.4)	0.03*
Smoking habits, %			
Never	28.7	23.6	0.21†
Former	48.3	57.5	
Current (1–34/day)	19.0	12.9	
Current (≥35/day)	4.1	6.0	
Mean (SEM)			
Alcohol consumption			
Frequency‡, n/month	15.6 (1.89)	9.5 (1.25)	0.02*
median	0.85	0	
Intake, g/day	11.1 (1.19)	7.0 (1.60)	0.02*
median	0	0	
Race/ethnicity, %			
Non-Hispanic white	85.9	86.2	0.17†
Non-Hispanic black	6.9	7.5	
Mexican-American	1.9	3.7	
Others	5.5	2.6	
Physical activity¶, mean (SEM) times/week			
Moderate + vigorous	6.90 (0.35)	5.97 (0.63)	0.24*
median	5.23	4.11	
Vigorous	3.58 (0.26)	3.18 (0.35)	0.46*
median	0.42	0.75	

*All percentages and means are calculated using sampling weights; adjusted for age; *t-test; †chi-square test; ‡assessed by food frequency questionnaire during the household interview; ¶assessed by 24-h recall during the physical examination (see text).*

FIG. 1. Age- and race-adjusted OR of LUTS by walking (miles/week) in men aged ≥60 years in the NHANES III, 1988–94.



adjusting for waist circumference, physical activity and cigarette smoking, or for hypertension. Using a second approach to assess alcohol consumption by 24-h dietary recall, men with an alcohol intake of ≥38 g/day had a lower OR of LUTS (OR = 0.41, 95% CI 0.14–1.2, *P* trend 0.08) than men with no alcohol intake.

Men who reported no leisure-time physical activity had a significantly higher odds of LUTS (OR = 2.09, 95% CI 0.14–1.2, *P* trend 0.08) than men who reported some physical activity, and adjusting for smoking, alcohol intake and waist circumference did not change this association. All levels of moderate or vigorous physical activity were also associated with a significantly lower odds of LUTS than men who reported no moderate or physical activity (Table 2). These results did not change after further adjusting for history of hypertension or for the presence of the metabolic syndrome (data not shown). However, vigorous physical activity alone was not consistently inversely associated with LUTS. The most frequently reported activity was walking. Fewer men with LUTS than men without reported walking (33.2% vs 50.8%, *P* = 0.003). Men who reported walking had a lower odds of LUTS than men who did not, although the OR did not decrease monotonically (Fig. 1). Adjusting for total frequency of moderate and vigorous physical activity as well as waist circumference, smoking and alcohol drinking did not change the association for walking.

DISCUSSION

In this group of older men in the USA, alcohol consumption and physical activity (moderate and vigorous) were both inversely associated with LUTS. Men who walked regularly were less likely to have LUTS than men who did not. There was no association between current cigarette smoking and LUTS, but we could not exclude that former heavy smokers were more likely to have LUTS.

Several studies have examined the association between cigarette smoking and LUTS, with inconsistent results. Most studies found no statistically significant association between cigarette smoking and LUTS [3–8], whereas three studies reported a statistically significantly positive association [9–11]. In an analysis of the Health Professionals Follow-up Study [11], heavy smokers had a significantly higher risk of LUTS than never smokers, whereas moderate smokers did not. Similarly, in NHANES III, there was no association for current cigarette smoking, but a suggestion of a higher occurrence of LUTS in heavier current, lifetime and former smokers.

There may be several explanations for LUTS possibly being more common in long-term heavy smokers. Nicotine increases sympathetic nervous system activity [17] and might contribute to LUTS via an increase in the tone of the prostate and bladder smooth muscle. Furthermore, smoking is thought to be associated with higher concentrations of testosterone [18]. A higher testosterone concentration might be associated with higher intraprostatic dihydrotestosterone levels, which is thought to be important in the development of BPH and LUTS [19].

There was a slightly greater chance of LUTS in former smokers and these men also had a higher odds of LUTS when they smoked ≥50 pack-years over their lifetime. Platz *et al.* [11] also reported a higher risk of LUTS in former smokers. The reasons for a greater risk of LUTS in former smokers are not clear. The greater waist circumference in former than in current smokers in this group of men might contribute to LUTS via increased insulin resistance [20]. Also, men who develop

symptoms might be more likely to stop smoking than men without symptoms. In addition, we cannot exclude chance as an explanation for this finding.

Men who frequently consumed alcohol were less likely to have LUTS than men who did not. There was also a lower odds of LUTS with increasing daily alcohol intake when using a second dietary assessment tool that captured intake the day before the interview. These results support the findings of two other studies reporting negative associations between alcohol consumption and LUTS [4,11], whereas the association was positive in two others [3,7]. Platz *et al.* [11] reported lower odds in moderate drinkers, but this protective effect was attenuated in men who consumed >50 g alcohol/day (≈ 3.5 or more drinks per day). This pattern was also apparent in another USA cohort study [9], in which African-American men with an intake of >72 g/day (five or more drinks per day) had a significantly higher odds of LUTS than non-drinkers, whereas there was no association in moderate consumers. Light to moderate alcohol consumption is associated with improved insulin sensitivity [21] and decreased testosterone concentration [22]. As an alternative explanation, we cannot exclude that the observed inverse association between the frequency of alcohol consumption and LUTS is caused by avoidance of fluids, especially of alcoholic beverages that have a diuretic effect, by men with LUTS, as there was an insignificantly lower odds of LUTS in men who drank caffeinated beverages at least four times a week (data not shown).

In NHANES III, men who were physically active in their leisure time were less likely to have LUTS. All levels of moderate and vigorous activity were inversely associated with LUTS, but the association for vigorous activity did not decrease consistently. Two previous studies reported inverse associations between the frequency of physical activity and LUTS [2,3].

Physical activity is associated with improved insulin sensitivity [23]. We previously reported statistically significant positive associations of glycosylated haemoglobin, a long-term marker of glucose and insulin metabolism, and the metabolic syndrome with LUTS in this group of men [24]. Alternatively, reductions in the odds of LUTS by physical activity might be caused by changes of sympathetic nervous system activity. Aerobic exercise training may elicit adaptations in the adrenergic system, because the sympathetic nervous system is activated through each bout of exercise, and repeated activation of this system could result in a reduction of the resting system activity [25]. In contrast to Platz *et al.* [2] there was no consistently inverse association between vigorous physical activity and LUTS in the

TABLE 2 The OR of LUTS by current smoking status, pack-years of smoking, alcohol consumption and physical exercise

Factor	OR (95% CI)*†	OR (95% CI)
Cigarette smoking status‡		
Never	1.00	1.00
Former	1.46 (0.88–2.40)	1.37 (0.79–2.36)
Current, cigarettes/day		
1–34	0.84 (0.46–1.54)	0.78 (0.39–1.56)
≥35	1.83 (0.74–4.53)	0.75 (0.31–1.82)
Pack-years of cigarette smoking		
All men		
Never	1.00	1.00
<21	1.27 (0.78–2.04)	1.22 (0.69–2.14)
21–49.9	1.10 (0.66–1.83)	1.22 (0.68–2.19)
≥50	1.72 (0.99–2.99)	1.43 (0.80–2.59)
Current smokers only		
Never	1.00	1.00
<21	0.52 (0.14–1.91)	0.64 (0.13–3.06)
21–49.9	1.08 (0.50–2.32)	0.78 (0.25–2.44)
≥50	1.19 (0.55–2.56)	1.08 (0.44–2.65)
Former smokers only		
Never	1.00	1.00
<21	1.34 (0.82–2.20)	1.21 (0.65–2.25)
21–49.9	1.07 (0.59–1.94)	1.22 (0.64–2.31)
≥50	2.16 (1.12–4.17)	1.91 (0.97–3.78)
Alcohol consumption, frequency§		
Never	1.00	1.00
<1/week	0.60 (0.33–1.09)	0.53 (0.24–1.18)
>1/week but <1/day	0.74 (0.37–1.45)	0.99 (0.47–2.08)
≥1/day	0.59 (0.36–0.97)	0.59 (0.34–1.03)
P trend	0.08	0.25
Frequency of physical activity, times/week¶		
Moderate and vigorous		
0	1.00	1.00
0.1–3.0	0.48 (0.24–0.99)	0.32 (0.14–0.74)
3.1–6.0	0.41 (0.18–0.91)	0.23 (0.09–0.57)
>6.0	0.49 (0.29–0.84)	0.35 (0.18–0.67)
P trend	0.05	0.07
Vigorous		
0	1.00	1.00
0.1–2.0	0.52 (0.25–1.10)	0.36 (0.15–0.87)
2.1–4.0	0.85 (0.40–1.82)	0.78 (0.32–1.88)
>4.0	0.80 (0.46–1.40)	0.77 (0.37–1.60)
P trend	0.88	0.80

**All results were calculated using sampling weights; †adjusted for age and race; ‡second column: smoking status: adjusted for age, race, frequency of moderate and vigorous physical activity, frequency of alcohol consumption and current waist circumference (continuous); §second column: alcohol consumption: adjusted for age, race, frequency of moderate and vigorous physical activity, smoking status and current walst circumference (continuous); ¶second column: physical activity: adjusted for age, race, frequency of alcohol consumption, smoking status and current waist circumference (continuous).*

present study. Only men who reported vigorous activity up to twice a week had a statistically significantly lower odds of LUTS, but the association was weaker in men who were more vigorously active. However, in this general population, few men reported participating in vigorous physical activity more than twice a week.

In addition to an inverse association between total moderate and vigorous activity, men who walked, the most often reported physical activity in this group of older men, were less likely to have LUTS. This association was reported previously in the Health Professionals Follow-up Study [2]. A small case-control study in Japan [26] reported that walking 10 000 steps or more per day for 12 weeks was inversely associated with sympathetic nervous activity and blood pressure in hypertensive men compared with sedentary men. Therefore, men who walk regularly might be less likely to have LUTS because of the lower tone of the prostate and bladder smooth muscle, and lower blood pressure, previously been shown to be positively associated with LUTS [9,20,24].

Several aspects of the study design merit further discussion. First, NHANES III is a cross-sectional study representative of the USA population of older men, thus aiding in the broad general applicability of these results. Also, the elderly were over-sampled, allowing for more stable estimates in the analysis of older men. Second, the questions on LUTS in NHANES III covered four of the seven questions of the AUA Symptom Index, which also includes frequency, intermittency and urgency, which together discriminated between men with and with no BPH in a clinical setting [13]. To increase the specificity of the present analysis, we included only men with three or four symptoms in the case group; we exclude men with only one or two symptoms in the control or case group because individually these symptoms are not specific for LUTS. Third, we cannot completely exclude that some men in the control group did not report LUTS because they were taking medications to treat their symptoms. However, this is unlikely because NHANES III was conducted between 1988 and 1994, and medication for treating BPH symptoms was not approved until 1992 (finasteride) [27] and 1993 (terazosin) [28]. Finally, smoking, alcohol consumption and physical activity were assessed concurrently with LUTS. Therefore, the results reflect associations and are not necessarily causal.

In conclusion, physical activity, even moderate activity like walking, may be beneficial for LUTS. Additionally, moderate alcohol consumption might be associated with a reduction in the occurrence of LUTS, whereas heavy cigarette smoking in the past may increase the occurrence of LUTS in older men. Intervention studies are needed to determine whether the frequency of LUTS can be modulated by changes in these lifestyle factors.

ACKNOWLEDGEMENTS

Dr Rohrmann is supported by the Fund for Research and Progress in Urology, Johns Hopkins Medical Institutions. Dr Crespo is supported by DAMD grant no. 170210252 and NIH grant no. 1P20CA096256.

CONFLICT OF INTEREST

None declared. Source of funding: S. Rohrmann: post doc funding through discretionary funds in the Department of Urology – no project funding was needed.

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Abbreviations: **NHANES III**, Third National Health and Nutrition Examination Survey; **MET**, metabolic equivalent of the activity compared to at rest; **OR**, odds ratio.

The relationship of BMI and prostate cancer mortality in Black and White men:

Results from the National Health Interview Survey Mortality follow up

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Abstract:

The relationship between body markers (or body mass index (BMI)) with risk of fatal prostate cancer is not consistent across studies. We use data from a nationally representative sample of U.S. adults to statistically ascertain an optimal BMI value associated with lowest risk of inst. Ca. mortality in two cohorts of Black and White men 40 years and older. We compared the effectiveness of Cox Proportional Hazards models that assume a linear relationship between BMI and the risk of prostate cancer with models that assume a J-shaped relationship. Our study found that for Black males over 40 years of age, neither a linear nor J-shaped relationship yielded a statistically significant model. With White males over 40 years of age, assuming a linear relationship did not yield a statistically significant model ($p = 0.582$). When we assume a J-shaped relationship, the optimal change point where the risk of prostate cancer death is minimized occurs when the BMI is equal to 25.5, an inverse relationship was found with a p-value equal to 0.009. Among White males over 40 years of age with BMI values greater than 25.5, a direct relationship was found with a p-value equal to 0.017. Adjustment for other covariates such as education, physical activity, height, and age did not change the nature of the results. Hence, with this data set we found that for White males over 40 years of age, Cox Proportional Hazards models that assume a J-shaped relationship between BMI and prostate cancer death provide a much better fit than models assuming a linear relationship.

Introduction

The relationship between BMI and prostate cancer is inconsistent. Cohort and case-control studies involving diverse populations to determine the relationship between prostate cancer and BMI have yielded ___ results. Moreover, there have been few studies examining this relationship in racial and ethnic minorities. We use the National Health Information Survey (NHIS) data to examine the relationship between BMI and risk of prostate cancer for Black and White males. We explore the feasibility of using a J-shaped risk curve to determine the effect of BMI on risk. We propose to estimate the BMI value that minimizes risk.

A number of studies that examine the relationship between BMI and the risk of prostate cancer have shown either no relationship or an inverse relationship between these two factors. Lee and coworkers [1] examined the relationship between physical activity and prostate-cancer risk for men enrolled in the Harvard Alumni Study. During the 6-year follow-up, 439 of the 8,922 participants developed prostate cancer. The analysis showed no evidence that either physical activity or body weight played a role in prostate-cancer etiology. Nilson and Vatten [2] completed a 12-year follow-up of 22,248 Norwegian men and also found no relation between BMI and prostate cancer. Giovannucci and coworkers [3] studied 2,896 incidents of prostate cancer from the Health Professionals Followup Study and concluded that no relationship exists between BMI and prostate cancer among older males (age $\geq$ 60 years). They found, however, that younger males with lower BMIs (what cutoff BMI < XX) exhibited a higher risk of

prostate cancer than did their counterparts with higher BMIs (BMI XX), showing an inverse relationship between BMI and prostate cancer risk for younger males.

Other studies have found a positive relationship between BMI and prostate cancer. Rodriguez and coworkers [4] examined BMI, height, and prostate-cancer mortality in two large cohorts of men selected from the Cancer Prevention Study I (CPS-I), who were enrolled in 1959 and followed through 1972, and from the Cancer Prevention Study II (CPS-II), who were enrolled in 1982 and followed through 1996. After exclusions, 1,590 prostate-cancer deaths remained among 381,638 men in CPS-I and 3,622 deaths, among 434,630 men in CPS-II. The investigators used Cox proportional hazards modeling to compute rate ratios (RR) and adjust for confounders. They found prostate-cancer mortality rates to be significantly higher among obese men (BMI $\geq$ 30).

Other studies [5, 6, 7, 8, 9] have found a positive relationship between BMI and prostate cancer while other studies [10, 11, 12] have found no relationship.

In 1997, Durazo and coworkers showed that the relationship between BMI and overall death can be modeled effectively using a J-shaped risk curve [13]. To our knowledge, no study has formally considered the use of a J-shaped curve to model the relationship between BMI and a prostate cancer. Goetghebeur and Pocock [14] have suggested an algorithm for determining when the use of a J-shaped curve is appropriate, along with a procedure for modeling when it is appropriate. For our analysis, we examine the risk of fatal prostate cancer for Black and White males over 40 years of age using a national representative sample of US adults who took part in the National Health Interview Survey from 1986 to 1994, and explore the appropriateness of employing a J-

shaped curve to explain the relationship between BMI and fatal prostate cancer. We also compare models that assume a J-shaped curve with those that do not.

B Methods

B.1 Data

We used data from the NHIS, a continuing nationwide survey of the U.S. civilian, non-institutionalized population conducted through households. Data from NHIS is used to monitor the health of the nation and to update many of the Healthy People 2010 national objectives. Detailed information about NHIS is described elsewhere. The average annual sample consists of 92,000 to 125,000 with a response rate of over 95 percent. Health and utilization variables include self reported age, height, weight, level of physical activity, family income, level of education, and self-assessed health status. To insure accuracy, a five-percent sample of all questionnaires is recoded and keyed by other coders. A 100 percent verification procedure is used if certain error tolerances are exceeded. The National Death Index is a repository of death certificate information from all U.S. states, Puerto Rico and other territories.

Linkage of NHIS respondents with the National Death Index from 1986 through 1997 has provided multiple cause-of-death data for NHIS survey years 1986-1994. The NCHS (spell out) uses a modification of a probabilistic approach to classify the NHIS-NDI potential matches. Our analysis used only cases with the highest probability of a match between NHIS respondents and NDI death data [15, 16]. More complete NHIS implementation procedures and linkage methodology are available at their website (www.cdc.gov/nchs/nhis.htm). For this study only White and Black males over 40 years of age with known BMI values were included.

B.2 Statistical methods

We examine the number of people classified by age and race who died from prostate cancer, who died from other causes, and who are still living, as well as the average BMI, average family income and average education for each of these sub-populations.

We also tabulated the rate and age adjusted rate for prostate cancer deaths and deaths from other causes by race and quartile of BMI. The values for the endpoints for the quartiles of BMI were generated for White males over 40 years of age and for Black males over 40 years of age from the BMI values which separated the respective populations into four equal parts.

To determine whether a J-shaped risk curve may be appropriate to describe the relationship between BMI and the risk of death from prostate cancer, we graphed cumulative death rates (calculated as 1-the Kaplan Meier survival rates) for the four quartiles of BMI. These curves were generated for Blacks and Whites adjusted for age using a Cox proportional hazards model [17].

A J-shaped risk curve is characterized by a change point where the relationship between BMI and risk of death from prostate cancer changes from varying inversely to varying directly. To find the value for this change point for White males and for Black males, we followed the procedure described by Goetghebeur and Pocack [14].

To compare models assuming linear and J-shaped relationships between BMI and the risk of prostate-cancer death, we fitted Cox proportional hazards models using BMI and age to predict survival time from prostate cancer for six populations: White males over 40 years of age, White males over 40 years of age with BMI values above the change point, White males over 40 years of age with BMI values below the change point

Black males over 40 years of age, Black males over 40 years of age with BMI values above the change point, and Black males over 40 years of age with BMI values below the change point. We then used the likelihood ratio (LR) tests to determine the nature and the magnitude of the effect of BMI on the risk of death from prostate cancer for these populations. These Cox models and the LR tests were performed both without adjustment and adjusting for education, family income, physical activity, and height.

High prostate cancer mortality rates among those with low BMI values may be a result of systemic weight loss in response to illness. To determine the effect of imminent death on the relationship between BMI values and death from prostate cancer, we removed deaths that occurred within three years of the interview and repeated our analyses with this reduced population.

C Results

Table 1 shows a description of the number of cases, the average BMI, the average income and the average education for prostate cancer deaths, other deaths, and those living by age and race.

Table 2 shows the rate and age adjusted rate of deaths from prostate cancer and deaths from all other causes by race and quartiles of BMI. For White males, when adjusted for age, the second quartile of BMI values has the lowest risk of death from prostate cancer and the third quartile of BMI values has the lowest risk of death from other causes. For Black males, the third quartile of BMI values has the lowest risk of both prostate cancer death and deaths from other causes.

Figure 1 shows the death rate (calculated as 1-Kaplan Meier Survival Rate) adjusted for age for the four quartiles of BMI among Black males. During the first seven

years of the follow-up the highest death rates occur in the first and fourth quartiles. This decrease and subsequent increase in the death rate as BMI increases indicates a J-shaped curve may be appropriate to model the relation between BMI and the risk of prostate cancer death. After the seventh year of the follow-up, there is no justification for a J-shaped relationship.

As can be seen in Table 1, there are few reported cases of prostate cancer among Black males. Hence, there is the possibility that excessive censoring may affect the later years of the follow up. When considering the entire follow up, we found no statistically significant model, neither linear nor J-shaped, to associate BMI with the risk of death from prostate cancer among Black males. Restricting our follow up to the first seven years, we also found no statistically significant model, neither linear nor J-shaped, to associate BMI with the risk of death from prostate cancer in this group of men. Hence, for Black males over 40 years of age we were unable to find any relationship between BMI and the risk of prostate cancer.

Figure 2 presents the same information for White males. This time the first and fourth quartiles have the highest death rates due to prostate cancer for the entire follow-up. Hence a J-shaped curve may be appropriate to describe the relationship between BMI and the risk of prostate cancer death [14].

When the estimated cumulative incidence (check working with Dan Sr; can we say incidence when we're studying mortality?) with competing risks was graphed, the rates were slightly lower; however, there was no significant change in the nature of the curves (data not shown).

Our analysis of the quartiles indicate that the relationship between BMI and the risk of prostate cancer in White males may follow a J-shaped curve which in turn, implies a BMI value that minimizes risk. We found that a BMI value of 25.5 should minimize the risk of prostate cancer death. We then fitted Cox proportional hazards model in three separate populations: all White males over 40 years of age, White males over 40 years of age with BMI ≤ 25.5, and White males over 40 years of age with BMI ≥ 25.5. Table 3 shows the results of these three Cox proportional hazard models using age and BMI to predict survival time for prostate cancer. When all White males over 40 years of age are included, the model shows that as BMI increases, the risk of prostate cancer death declines. However, both the confidence interval and the p-value indicate that the overall inverse relationship determined by this model is not statistically significant. When only White males over 40 years of age with BMI values greater than 25.5 are included, the model shows that as BMI increases, the risk of prostate cancer grows. Both the likelihood ratio test and the confidence interval indicate that this positive relationship is statistically significant. When only White males over 40 years of age with BMI values less than 25.5 are included, the model shows that as BMI increases, the risk of prostate cancer diminishes, and both the likelihood ratio test and the confidence interval indicate that this inverse relationship is statistically significant. Hence, these models support a J-shaped curve to describe the relationship between BMI values and the risk of prostate cancer in White males 40 years of age and older.

We performed the same analyses outlined in the previous paragraph on Black males over 40 years of age. However, no statistically significant models ($p < 0.05$) were found and the data did not suggest a J-shaped curve was more appropriate than a linear

curve for modeling the relationship between BMI and the risk of death from prostate cancer (data not shown).

In Table 4, we present the results when the procedures used to generate Table 3 are adjusted for education, family income, physical activity, and height. The minimum risk of prostate cancer is found at a BMI value of 24.9 instead of 25.5. A linear model that does not assume a minimum risk is not statistically significant. If we assume a minimum risk and separately model each side of this minimum, we obtain two statistically significant models. Hence, while the adjusted models are slightly less significant than the unadjusted models, the general nature of the relationship between BMI and the risk of prostate cancer death does not change when we adjust for these variables.

High mortality rates among those with low BMI values could be due to systemic weight loss in response to a disease. Table 5 presents the same data as Table 3 when all deaths within 3 years are removed from the population. As 40 percent of prostate deaths were removed from the population, the statistical significance of all models was reduced. However, the inverse relationship between BMI values and the risk of prostate cancer death for White males with BMI less than 25.5 remained statistically significant (p = 0.04) which would suggest that the J-shaped relationship is not solely the result of systemic weight loss in response to illness.

D Discussion

The overall rate of death due to prostate cancer for males over 40 was greater than 1 percent among Blacks and slightly less than 0.5 percent among Whites. White men who died from prostate cancer had considerably higher education and income and lower BMI

values than their Black counterparts of the same age group. However, prostate cancer victims had incomes and BMI values very similar to their living counterparts of the same race and age group. The education of victims of prostate cancer tended to be lower than their living counterparts of the same race and age group.

Our findings do not support a J-shaped curve in this population. Relationship between BMI and fatal prostate cancer from Black men, but it does for White men. Applying a LR test with a Cox proportional hazards model using BMI to predict survival time among Black males with age as a covariate found insufficient evidence to assume a relationship between BMI and risk of death from prostate cancer. Although the rate of prostate cancer is far higher for Black males than for White males, our analytic sample had fewer Black males that died of prostate cancer than White males. Hence, our inconclusive results for Black males are not necessarily indicative that a relationship between BMI and prostate cancer does not exist, but that we did not have enough power to find a relationship.

Our findings are the first one to statistically test a J-shape curve to describe prostate-cancer risk due to BMI. However, data from several studies suggest that the risk of prostate cancer due to BMI first lowers as BMI increases and then rises as BMI increases further. Nilson and coworkers [2] in their study of 22,248 Norwegian men found that the lowest risk of prostate cancer was associated with BMI values between 23.1 and 24.7. Nomura and coworkers [11] in a study of 8,006 Japanese men from 1965 to 1968 found that the minimum risk of prostate cancer was for males whose BMI values were in the second quintile. Hsing and coworkers [18] in the their study of 238 cases of newly diagnosed prostate cancer included BMI and history of BMI in their analysis. For

current BMI values, the minimum risk of prostate cancer occurred in the third quartile of BMI. Historical evidence indicated that for 20-29 year olds, the lowest long term risk of prostate cancer occurred for those with BMI values in the first quartile ___ (xx-xx). However, for all other historical age ranges presented, people with BMI values in the second or third quartile had the lowest long term risk of contracting prostate cancer.

In studies where the minimum risk of prostate cancer as related to BMI occurred in the 2^{nd} or 3^{rd} quartile, the investigators concluded that there was no relationship between BMI and risk of prostate cancer. Our analysis of the NHIS data also produced this negative result before we modeled using a J-shaped curve. Given our finding, some of the negative results of these earlier studies may reflect their not having considered the possibility of a J-shaped relationship.

Other studies [19, 20] that found no relationship between BMI and the risk of prostate cancer reached this conclusion because there was no statistically significant difference between the mean BMI values of males that developed prostate cancer and the mean BMI values of males that did not develop prostate cancer. Our experience with the NHIS data also indicated that there was no statistically significant difference between the mean BMI values of males that developed prostate cancer and the males that did not develop prostate cancer. Correspondingly, these datasets may also warrant further analysis.

When we fitted the Cox proportional hazards model without assuming a J-shaped curve, the Hazard ratio was almost equal to one. Therefore, if a J-shaped curve is not assumed, the data do not support a relationship between BMI and the risk of prostate cancer death. However, when we determined a change point value, two statistically

significant models (p-values < 0.02) were produced for the populations on each side of the change point. More importantly, this relationship does not significantly change when controlled for education, income, height, and physical activity. As the inverse relationship between lower BMI values and risk of prostate cancer death remains statistically significant when deaths occurring within three years of the interview are removed from the population, response to an illness alone does not appear to explain the relationship.

In conclusion, we found that among White males over 40 years of age, only assuming a J-shaped curve could we produce statistically significant models. As the inverse relationship between the risk of prostate cancer and low BMI persisted when deaths within three years of the interview were removed, imminent death alone does not explain the J-shaped relationship between BMI and the risk of prostate cancer death. Among White males over 40 years of age we found a J-shaped curve relationship between BMI and fatal prostate cancer. The lowest risk was observed for BMI of 25.5 (age-adjusted). Adjustments for other important covariates such as physical activity, education, height and income did not change the nature of the relationship, only the BMI cutoff point to 24.7.

The nature of the relationship could not be reproduced among Black males. Increase prostate cancer mortality among those with lower BMI may not be entirely explained by preexisting conditions as the results were similar after deletion of all mortality cases in the first three year of follow up.

Our findings support a closer look at other data sets that have not tested for a J-shape curve to better understand the relationship between BMI and prostate cancer mortality.

A possible biological plausibility of our findings may be the presence of circulating testosterone hormones at different BMI levels, an also of possible racial differences in the relationship between BMI and adipose tissue. A limitation of our results is that they are based on self reported height and weight and the possibility of underreporting of body weight.

Future studies should consider examining obesity and prostate cancer mortality among Black and White populations of different BMI to more clearly determine optimal BMI values associated with reduced risk for prostate cancer.

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Figure 1. Age adjusted death rates from prostate cancer among Black men according to quartiles of BMI at baseline. Results from the National Health Interview Survey Mortality Follow up.

Figure 2. Age adjusted death rates from prostate cancer among White men according to quartile 2 and quartile 4 of BMI at baseline. Results from the National Health Interview Survey Mortality Follow up.

Figure 3. Age adjusted death rates from prostate cancer among White men according to quartile 1 and quartile 2 of BMI at baseline. Results from the National Health Interview Survey Mortality Follow up.

Figures and Tables

Average BMI for Prostate Cancer Deaths and Others by Race and Age Group

African Americans

Age	Prostate Deaths			Other Deaths			Living		
	n	mean	sd	N	mean	sd	n	mean	sd
40 - 49	1	33.064		423	27.306	6.179	6132	27.337	4.5095
50 - 59	21	28.891	5.1544	640	26.99	5.3556	4174	27.74	4.6652
60 - 69	63	27.137	4.7205	1066	26.528	4.8756	3091	27.332	4.277
70 - 79	79	26.765	4.7739	902	25.508	4.5104	1398	26.547	4.2563
>79	36	24.682	4.5484	474	24.619	4.3656	325	25.185	3.9395

Caucasians

Age	Prostate Deaths			Other Deaths			Living		
	n	mean	sd	N	mean	sd	n	mean	Sd
40 - 49	11	28.459	5.0952	1375	27.473	5.3971	44865	27.216	4.2721
50 - 59	27	26.979	3.9029	2718	27.151	4.8893	30616	27.336	4.0416
60 - 69	175	27.308	4.3394	5633	26.605	4.5788	24121	26.992	3.8106
70 - 79	290	25.626	3.8819	6926	25.608	4.0535	12262	26.212	3.5513
>79	178	24.279	3.6901	4058	24.159	3.6665	2639	25.2	3.3536

Table 1

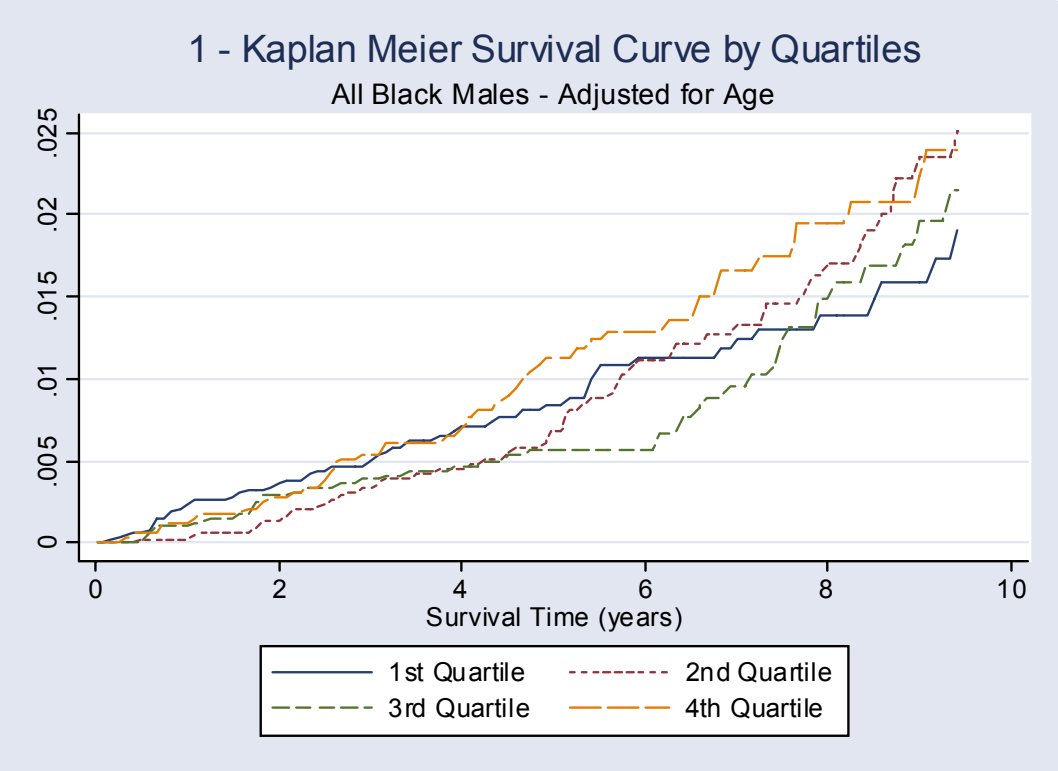
1 - Kaplan Meier Survival Curve by Quartiles
All Black Males - Adjusted for Age
0
.005
.01
.015
.02
.025
0
2
4
6
8
10
Survival Time (years)
1st Quartile
2nd Quartile
3rd Quartile
4th Quartile

Figure 1

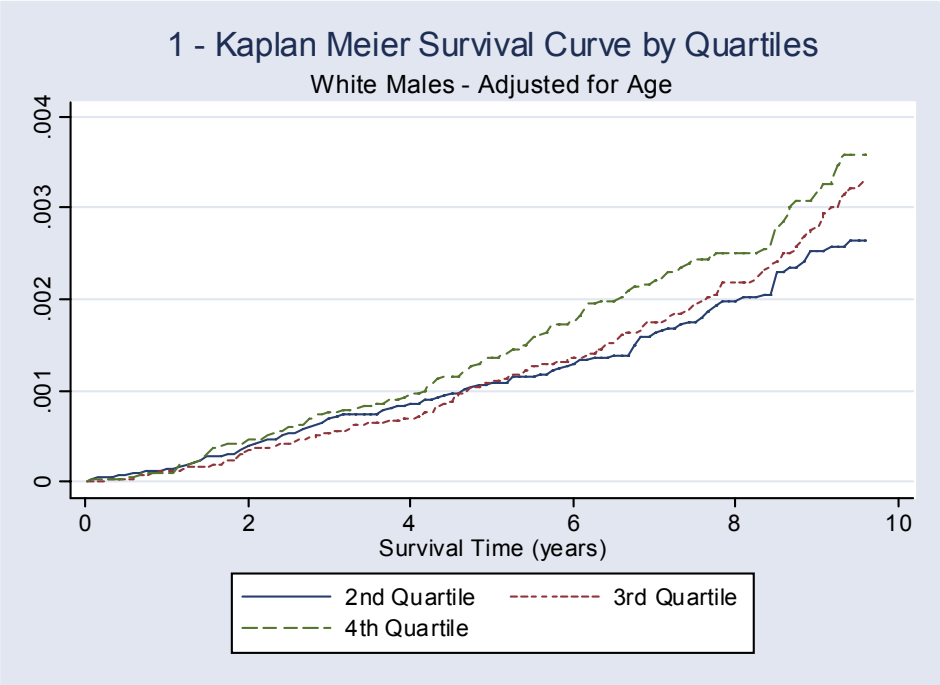
1 - Kaplan Meier Survival Curve by Quartiles
White Males - Adjusted for Age
0
.001
.002
.003
.004
0
2
4
6
8
10
Survival Time (years)
2nd Quartile
3rd Quartile
4th Quartile

Figure 2

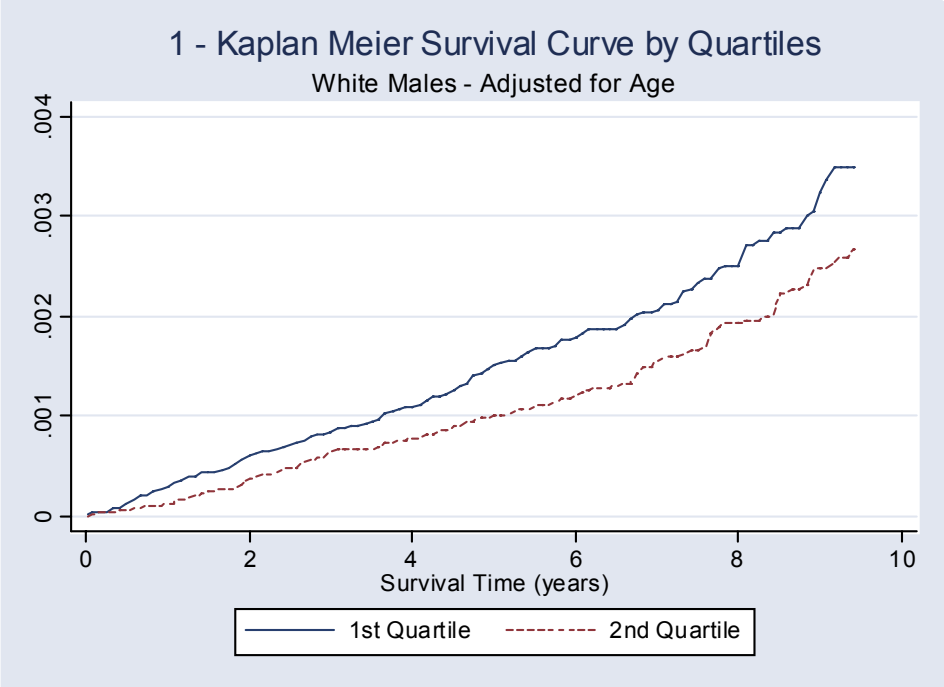
1 - Kaplan Meier Survival Curve by Quartiles
White Males - Adjusted for Age
0
.001
.002
.003
.004
0
2
4
6
8
10
Survival Time (years)
1st Quartile
2nd Quartile

Figure 3

Quartile	Deaths	N	Rate	Age Adjusted Rate	SE(AAR)	95% Confidence Interval
1	7,855	34,875	0.225	0.186	0.00083	0.1845 - 0.1878
2	4,834	34,467	0.140	0.141	0.00074	0.1396 - 0.1426
3	4,156	31,793	0.131	0.139	0.00077	0.1371 - 0.1401
4	4,304	33,445	0.129	0.153	0.00080	0.1516 - 0.1548

Table 2

Obesity as a predictor of prostate cancer mortality in Puerto Rican men.

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Portland State University, Florida State University, Harvard University and University of Puerto Rico

Background: Obesity has been linked to several chronic diseases, including mortality from selected cancers. The association between excess body weight and adult weight gain has been linked to prostate cancer in some studies but not all. Prostate cancer mortality among Hispanics is similar to those of non-Hispanic whites in the US, however, prostate cancer kills more Puerto Ricans than any other cancer. The purpose of this study is to prospectively examine the relationship between obesity and fatal prostate cancer among Puerto Rican men.

Methods: We used data from the Puerto Rico Heart Health Program, a longitudinal study of 9824 men aged 35-74 years who were examined at baseline for coronary heart disease risk factors. Body weight and height were ascertained through a physical examination at baseline. We classified this cohort of men based on baseline body mass index (wt/ht2) using the WHO classification. Prostate cancer mortality was obtained through linkage with the Puerto Rico Cancer Registry and the Puerto Rico Vital Statistics Registry. Multivariate logistic regression was used to estimate the Odds Ratios and 95% confidence interval of fatal prostate cancer mortality among underweight (BMI<18.5), overweight (BMI=24.5-29.9), and obese (BMI>=30) participants compared with healthy weight (BMI=18.5-24.9).

Results:
We found 167 prostate cancer cases. Using participants with a healthy weight as the reference (N=76), the age-adjusted risk for fatal prostate cancer for the following groups were underweight (N=4), OR=0.70 (CI=0.25, 1.93, P=0.499); overweight (N=66), OR=1.11 (CI=0.79, 1.55, P=0.548); and obese (N=21), OR= 1.10 (CI=0.67, 1.79, P=0.707). Adjusting for other covariates such as physical activity, education and smoking did not significantly alter the findings. Our results support the hypothesis that obesity is not a risk factor for prostate cancer mortality in this group of Puerto Rican men. Moreover, additional analysis on age-stratified weight gain based on self-report body weight at age 25 years, and body weight at baseline do not support an association between weight gain and fatal prostate cancer either.

Conclussion:
While some studies have found a significant relationship between prostate cancer risk and body weight, our results do not support such a relationship. Additional research is needed to also include better measures of other health indicators that accompany weight gain such as physical inactivity, diet, smoking and other potential deleterious lifestyle that may be linked with prostate cancer mortality.

This work was supported by a grant from the Department of Defense (DAMD17-02-1-0252).

Urban Living and Risk of Fatal Prostate Cancer among Puerto Rican Men: The Puerto Rico Heart Health Program.

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Purpose: Prostate Cancer is the leading cause of cancer deaths in the commonwealth of Puerto Rico. We assessed the association of urban residence with the risk of fatal prostate cancer in a population-based cohort of Puerto Rican men.

Methods: The Puerto Rico Heart Health Program (PRHHP) is a prospective cohort study designed to examine morbidity and mortality from coronary heart disease among Puerto Rican men. The cohort included 9,824 men, aged 35-75 years free of coronary heart disease at baseline. The sample was randomly selected from four rural municipalities (Naranjito, Comerio, Barranquitas, and Corozal), and three urban municipalities (Bayamon, Guaynabo, and Carolina). The baseline exam was conducted during the years 1965-1968. There were three subsequent exams, which took place during the years 1968-71, 1971-75, and 1974-77. For this study participants completed an extensive self-report of demographic characteristics, personal and family health history, and health habits. Mortality status and cause of death were ascertained by matching participants in the PRHHP with electronic files from the Puerto Rico Cancer Registry and Puerto Rico Vital Statistics Registry. Records for cohort members were obtained based on a full match of first name, maternal and paternal last names, date of birth, place of birth, and gender. The present analysis includes 9803 participants with complete data. There were 2829 ascertained deaths as of June of 2002; of these, 124 had prostate cancer listed as a cause of death on the death certificate. We conducted univariate and multivariate logistic regression analysis to assess the association of urban residence with risk of prostate cancer mortality. Other covariates included, education, smoking, body mass index, physical activity and skinfold measurements.

Results: In a multivariate model that adjusted for age, the odds ratio associated with urban residence was 1.56 (95% CI: 1.02, 2.39, p=0.04).

Conclusions: In this cohort of Puerto Rican men, urban residence was associated with a 50% increase in risk of fatal prostate cancer. Further research should investigate other environmental factors that may be associated with increase the risk of prostate cancer among urban dwellers.

This work was partially supported by grants from the Department of Defense (DAMD17-02-1-0252), and the National Institutes of Health (1P20CA96256-01A1, 1R03 CA103475-01).